

TROPICAL DISEASES
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SUMMARY OF RECENT ABSTRACTS*

I CHOLERA

Very little work on cholera has been reported in the period under review but for the sake of continuity the information available is summarized in the usual way

Epidemiology and Bacteriology

Investigations into the endemicity of cholera in Bengal and Madras are being carried out under the auspices of the Indian Research Fund Association (p 39). In Tanjore the mortality has decreased between 1930 and 1941 but the enquiry is to be continued in certain small areas suitable for this kind of study. The districts should be homogeneous in respect of their cholera history and a number of taluks have been chosen, which satisfy the requirements and in which the studies will be made.

The Scientific Advisory Board of the Indian Research Fund Association (p 39) reports that Inaba and Ogawa subtypes of *V. cholerae* have been isolated from water of the Hooghly river. 15 of 644 samples were positive isolation being made by the candle-boric-peptone-water method [see this *Bulletin* 1943 v 40 241]. The majority of the samples tested were positive for non-agglutinating vibrios. The same method gave much better results in isolation from cholera stools than did direct plating on bile-salt agar or the Wilson and Blair medium. Cholera vibrios added to Hooghly water could not be isolated from it after a period of 3-4 days but when the water had previously been filtered they could be isolated up to the third week.

PANJA and GHOSH (p 40) have shown that brilliant green, malachite green, crystal violet and methylene violet have a selective bactericidal action *in vitro* on most Inaba and Ogawa subtypes of *V. cholerae*. Thus brilliant green at a dilution of 1 in 100 000 exerted a completely selective bactericidal effect on those subtypes, being harmless to non-agglutinating vibrios isolated from Hooghly water. Cholera patients have been treated with brilliant green by the mouth but although vibrios disappeared early from the stools clinical improvement was not especially marked.

SEN GUPTA (p. 401) shows that in the Calcutta area, during the past few years there has been a very decided swing towards preponderance of the Ogawa

*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1944 v 41. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

subtype of *V. cholerae* in isolations made from cases of cholera in 1943 only 1 Inaba strain was recovered, against 154 Ogawa. The matter is held to be important in its bearing on the subtypes from which vaccine should be prepared, and the author makes the point that during epidemics great care should be taken to determine the prevalent subtype so that an appropriate vaccine can be made.

GALLT has previously shown that the cholera vibrio contains a glucolipid complex which is the somatic O antigen, and that the toxin itself contains both glucolipidic and protein active elements. As a result of quantitative studies on the precipitation of the glucolipidic antigen by antiserum, this author with GRABAR (p. 401) has found notable differences in the immunological behaviour of vibrios belonging even to the same serological group, which may form the basis of a classification of cholera vibrios in general. The same authors (p. 402) have found that the cholera toxin contains no antigen other than the glucolipid. When first elaborated the toxin apparently contains a complex glucolipid antigen, which is subsequently split into a simpler glucolipid (such as that of the extract of the vibrios) and a substance which is not precipitated by the immune serum.

GALLT and BRUNER (p. 848) have found, in animals immunized with O and OH cholera vaccine (Inaba 5 type) that agglutination of the homologous vibrio occurs within a few minutes if the vibrio suspension is mixed with whole blood of the immunized animal. The vibrio suspension is heated at 56°C. for the O antigen and at 100°C. for 2 hours (or the glucolipidic antigen is used) for the OH antigen. The suspension after filtration through cotton wool, is coloured with methylene blue to facilitate reading of the test. It is possible that agglutination with whole blood instead of serum, will be found useful in human cholera, especially in cases in which serological methods give equivocal results in other diseases for instance the enteric fevers and typhus, in which whole blood agglutination has been compared with serum tests, the evidence is, in general, in favour of the whole blood test. Incidentally the authors found that intravenous injection of the vaccines produced, in rabbits, better immunological response than subcutaneous injections.

Clinical Findings and Treatment.

In the Report of the Scientific Advisory Board of the Indian Research Fund Association for 1942 (p. 39) is a brief mention of the treatment of cholera with sulphaguanidine. No claims are made, but the results appear to be favourable enough for the trials to be continued. Investigation of the value of sulphaguanidine is also in progress. All agglutinating vibrios are very susceptible to brilliant green and malachite green, and administration of the former (1 in 2,500 dilution, but the actual dose is not stated) to cholera patients caused the vibrios to disappear from the stools more quickly than they disappeared in controls not treated with the dye.

HICKEY (p. 849) writes in very favourable terms of the value of sulphaguanidine in the treatment of cholera, especially when combined with injection of saline. He records 22 cases so treated, only one patient died. The dosage was as follows—sulphaguanidine 3 gm. as a first dose followed by 1 gm. every 2 hours for 6 doses, then 1 gm. every 4 hours for 1-2 days. The number of cases is admittedly small, but the results appear to have been striking.

WEXDEMORF (p. 130) has described three cases in which there was, apparently hypersensitivity to the protein of *V. cholerae* this was shown by severe systemic reaction to the injection of cholera vaccine.

Charles Wilcock.

MALARIA.

- i RIBBANDS C. R. Differences between *Anopheles melas* (*A. gambiae* var *melas*) and *Anopheles gambiae* 1.—The Larval Pecten. *Ann Trop Med & Parasit* 1944 Sept. 30 v 38 No 2 85-6 2 figs.
- ii — Differences between *Anopheles melas* and *Anopheles gambiae* II.—Salinity Relations of Larvae and Maxillary Palp Banding of Adult Females. *Ibid* 87-99 2 figs. [15 refs.]

i. In the past *Anopheles melas* has been regarded as a variety of *A. gambiae* produced, it was supposed when the larva had developed in highly saline water. In these two papers the author establishes that *A. melas* is a distinct species. There are constant differences between the eggs of the two mosquitoes (THOMSON unpublished observations). In the first paper here reviewed it is shown that there are constant differences in the larval pecten—all families resistant to salinity had pectens of the *melas* type (with more or less even teeth)—the pectens of all non-resistant families were of the *gambiae* type (with a number of long teeth interspersed among the shorter teeth).

ii In the second paper it is shown that the palpal banding of the adult female is not a constant character. Only 54 per cent of true *melas* (as determined by the larval pecten and by their resistance to high salinity) were recognizable as such from the palpal bands when reared in the laboratory (far fewer will be recognizable in the wild population). The marking of the palps varies from the typical *gambiae* type to the extreme *melas* type in single families—and the proportion of the *melas* type varies widely from one family to another and probably in different populations. There was no correlation between the proportion of *A. melas* with extra dark markings on the palps and the salinity of the water in which they had been reared. The differences are truly genetic. *A. gambiae* will develop from egg to adult in 37½ per cent sea water (11.9 gm NaCl per litre) or 60 per cent, if they are accustomed to it gradually. *A. melas* will develop completely in 150 per cent sea water (47.6 gm NaCl per litre); many larvae will survive transfer to 225 per cent (71.3 gm NaCl per litre). A practical test for distinguishing the two larvae has been evolved. Batches of mixed larvae are transferred to 37½ per cent sea water for one day and then to 75 per cent sea water on the second day. *A. melas* larvae survive. *A. gambiae* are eliminated by the end of the second day. The difficulty in distinguishing the adults of the two species is unfortunate because it is important to know what proportion of malaria transmission in a locality is due to *gambiae* and how much due to *melas*—for the breeding places of *gambiae* are small, concentrated and easily recognized whereas those of *melas* are so large and sparsely populated by larvae that they may be overlooked.

V B Wigglesworth

ULITCHEVA, A. V. [Anophelogenous Role of the various Types of Waters of a Rice Region] *Med Parasit & Parasitic Dis* Moscow 1943 v 11 No 6 33-47 7 graphs

An abstract of this paper is published in *Rev Applied Entom* Ser B. 1944 Sept. v 32, Pt. 9 169-70

ULITCHEVA, A. V. [Distribution of the Larvae of *Anopheles maculipennis sacharovi* through a Rice-Field (Samarkand District)] *Med Parasit & Parasitic Dis* Moscow 1943 v 11 No 6 47-52, 3 graphs

An abstract of this paper is published in *Rev Applied Entom* Ser B. 1944 Sept. v 32, Pt. 9 170-71

ULITCHOVA, A. V. [The Ecology of the *Anopheles* Larvae in Rice-Fields of various Types in Uzbekistan.] *Med. Parasit. & Parasite Dis.* Moscow 1943 v 11 No. 6 53-61

An abstract of this paper is published in *Rev. Applied Entom.* Ser. B. 1944 Sept., v 32, Pt 9 171-2.

GALVÃO A. L. A. CORRÊA, R. R. & GRIZCO S. J. Alguns dados sobre a manutenção de colônias de *Nyssorhynchus* em laboratório. [Rearing and Maintaining *Anophelines* in the Laboratory] *Arquivos de Hig. e Saúde Pública.* 1944 Jan. v 9 No. 20 85-102, 10 figs. English summary (7 lines) p. 96.

The authors have confirmed the work of BORD CAIX and MULEKIAN (see this *Bulletin* 1935 v 32, 806) who stressed the facts that success in rearing mosquito larvae depends upon an abundant supply of the proper food and the maintenance of temperature constantly at an optimal level. In order to test the therapeutic value of drugs in experimentally transmitted malaria the authors wished to rear and maintain efficient vectors namely *A. allatensis domesticus*, *A. argyritarsis* and *A. larviculatus*. With this end in view they adopted the original method of Bord and his colleagues with certain minor modifications which are described. These have regard to the food, the temperature and the breeding room and cannot be abstracted. Those interested should consult the original which is well illustrated. Their colonies are being maintained and so far they have bred the first named to the seventh generation, the second to the sixth and the third to the fifth.

H. Harold Scott

GLASGOW R. D. & BLAIR, R. The Use of Explosives for the Application of Insecticide Dusts. *J. Econom. Entom.* 1944 Apr. v 37 No. 2, 230-34 4 figs.

An account is given of some preliminary experiments in which insecticidal dusts were discharged from improvised mortars with the object of controlling caterpillars in the inaccessible parts of large trees. It is suggested that the method might be developed for applying larvicides under war conditions to the breeding places of mosquitoes which cannot readily be reached by other means. The breeding of *Anopheles bellator* in the epiphytes on the Immortelle which is grown as a shade tree in the cocoa plantations of Trinidad is given as an example.

I. B. Wigglesworth

SHEPHERD W. H. T. Radiological Estimation of Splenic Enlargement in Malignant Tertian Malaria. *Brit. J. Radiology* 1944 Sept. v 17 No. 201 230-85 9 figs.

A radiographic technique for demonstrating the spleen without the use of any contrast medium is described. This technique was then applied (a) to determine the size of the normal spleen (controls) (b) to determine the size of the spleen in clinically suspected malaria and (c) to determine the size at which the spleen becomes clinically palpable. It was hoped that from the second of these investigations some information might be derived which would assist in the diagnosis in doubtful cases.

The product of the length and breadth (measured in inches) of the shadow of the spleen was called the Radiographic Splenic Index.

It was concluded that the upper limit for the normal radiographic spleen was an index of 8. The index for the earliest degree of enlargement which could be detected clinically was 9½-10½. Fifteen cases of malaria showed a considerably raised splenic index in the region of 11-14½.

The author concludes that in cases in which the clinical diagnosis is doubtful and blood smears for malarial parasites are negative the radiographic splenic index may be of diagnostic value by demonstrating enlargements (not clinically appreciable) of the spleen

E Samud

HUNT T C. Medical Experiences in North Africa, 1943-4 *Brit Med J* 1944 Oct 14 495-8. [Malaria 496-7]

Nothing surprised me more about malaria in North Africa than its difference from malaria in West Africa. In North Africa we saw both benign tertian and malignant tertian. There were many relapse cases—some severe persistent and resistant to treatment—but in over 1 000 patients admitted to my division there was not a single death. This was certainly better than in West Africa where I had one death from cerebral malaria and one from blackwater fever in roughly the same number of cases but for clinical severity the M T malaria of North Africa was unquestionably the more alarming. In North Africa the condition was more polysymptomatic the need for treatment more urgent and the response often less satisfactory. Here intravenous quinine injections became a frequent and almost usual procedure while in West Africa it was rare. During the malaria season over 1 000 injections were given in my hospital with only minor symptoms on two or three occasions. This timely intravenous quinine no doubt saved many lives among desperate cases even though a considerable number would almost certainly have recovered with oral treatment alone. Of the many well known and important lessons about malaria—often learnt perhaps at a price—these were some that we learnt once more in North Africa.

1 In a malarious country headache is not to be regarded as due to psychoneurosis until malaria has been excluded

2 Malaria with low fever may be more dangerous than with high because it is more easily missed.

3 To wait for a positive blood slide or a palpable spleen costs more lives than to treat a suspicious case on an unproved diagnosis.

4 The exact date of onset of malaria is not the same thing as the date of admission to a medical unit where a man lives may be much more important than what he does.

5 To transfer a case of active malaria without treatment and without full precautions for continuation of treatment is a medical crime

6 Other diseases do not exclude malaria and malaria especially relapsing malaria has often some complicating disease

7 Diarrhoea with blood and fever is not always due to dysentery jaundice with fever is not always infective hepatitis malaria may mimic both. Asthma fibrositis neuritis urticaria, and nephritis are only some of the less well recognized conditions that malaria may cause while it may simulate at least a dozen others

GAYID I K. Some Notes on the Symptomatology and Treatment of Malaria. *J Roy Army Med Corps* 1944 July v 83 No. 1 28-33 4 charts.

These notes are the result of experience in a desert General Hospital of the Middle East Command. During 1942 dysentery (1,332 cases) and malaria (1 126 cases) were the most prevalent diseases treated. Ninety-two per cent. of the malaria cases occurred during the four months July to October the September total (440) being the highest.

In the author's experience *P. vivax* infections frequently fail to produce the characteristic regular febrile periodicity described in text books five illustrative cases are recorded. For a patient with irregular fever and enlarged spleen, and

a past history of malaria or exposure to malaria infection, anti-malarial treatment is indicated even if no parasites be found on blood examination. If there be no response to quinine, 10 grains thrice daily for two days the treatment should be stopped and the diagnosis reviewed. Malaria not uncommonly coexists with other infections.

The standard treatment of malaria in the Middle East has been quinine grains 10 thrice daily for 3 days mepacrine 0.1 gm. thrice daily for the next 5 days after 3 days without specific treatment pamaquin 0.01 gm. thrice daily for 3 days. If there be vomiting—or in heavy infections—the treatment is begun with one or two intramuscular injections of quinine 8 to 10 grains during the first day. Intravenous quinine should be used sparingly. It is advisable to give adrenaline at the same time, either intramuscularly or intravenously. The author advocates for intravenous administration 8 to 10 grains of quinine in 20 cc. of 25 to 50 per cent glucose solution. *Norman White*

RICO-ARIELLO C. Clínica atípica del paludismo marroquí. [Atypical Malaria in Morocco.] *Med Colonial* Madrid. 1944 July 10 v 4 No. 1 7-17

BALASQUIDE, L. A. La malaria en relación con la obstetricia y la ginecología. [Malaria in relation to Obstetrics and Gynaecology.] *Bolet. Asoc. Med. de Puerto Rico* 1944 June, v 36 No. 6 269-77 [18 refs.]

FINDLAY G M, MARKSON J L & HOLDEN J R. Investigations in the Chemotherapy of Malaria in West Africa. I. Treatment with Quinine and Mepacrine. *Ann. Trop. Med. & Parasit* 1944 Sept. 30 v 38 No. 2, 139-48.

The observations recorded in this paper were made in a West African Military Hospital. The patients were young adult European males who had not previously resided in the tropics. More than half of them were suffering from their first attack of malaria. Infection, *P. falciparum*, had been acquired in all parts of the four British West African colonies. There is some evidence that different strains of *P. falciparum* exist in West Africa. Africans from the Gold Coast stationed on the north bank of the Gambia River had a surprisingly high malaria-rate, and Belgian Congo African troops in Nigeria had a malaria rate three times as high as that of Nigerian troops stationed nearby.

With military patients in a hyperendemic area it is essential to avoid both under-treatment and over-treatment. There is no evidence that excessive dosage decreases the relapse rate. The impossibility in most cases, in hyperendemic malaria regions, of distinguishing reinfection from relapse makes it difficult to assess the value of a particular treatment in preventing the latter. Nevertheless the chances of a second attack of malaria in such areas are not very great. A random sample of British troops was carefully observed during 1943—the incidence of malaria was —

No. of British Officers and other ranks	No. with malaria	No. of attacks of malaria					
		1	2	3	4	5	6
2,441	538	395	89	39	12	3	1

Two-thirds of the patients had been treated with quinine and mepacrine and one third with mepacrine alone—there was no evidence that either treatment was more effective than the other in preventing return to hospital.

To determine whether mepacrine could be substituted entirely for quinine—and, if so the most suitable dose for the treatment of malaria in West Africa—

be entirely replaced by mepacrine. Quinine is reserved for cases of cerebral malaria, for hyperparasitism (15 per cent. or more of red cells parasitized) for the rare cases where temperatures of 103°-105°F have failed to react to mepacrine and for the still rarer cases in which mepacrine has caused vomiting or psychotic change.

Norman White

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To determine whether mepacrine could be substituted entirely for quinine—and, if so, the most suitable dose for the treatment of malaria in West Africa—140 patients with *P. falciparum* infections were treated as follows —

- (1) 20 patients quinine sulphate 30 grains daily for 6 days.
- (2) 40 patients quinine sulphate 30 grains daily for 2 days followed by mepacrine 0.3 gm. daily for 6 days
- (3) 40 patients mepacrine 0.3 gm. daily for 6 days
- (4) 20 patients mepacrine 0.6 gm. first day 0.4 gm. second day and third days 0.3 gm. on each of the next three days
- (5) 20 patients mepacrine 0.8 gm. the first day 0.4 gm. second and third days 0.3 gm. fourth, fifth and sixth days

Malaria parasites had been found in the peripheral blood of all these patients before treatment was begun. In a number of cases of clinical malaria in which no parasites could be found in the peripheral blood smears from sternal bone-marrow revealed their presence. There are no such cases in the present series. No selection of cases was made except that two patients with hyperparasitism were treated with intravenous quinine. Thick blood films were examined morning and evening. For parasite counts the number of parasites in 10 fields was counted (1/12 objective and $\times 8$ ocular). Parasites were not said to have disappeared from the blood until 100 fields had been examined with negative results. Quinine salts were given in solution, the dose being followed by a tumblerful of water. Mepacrine crushed up in fruit juice is a useful way in which to give the drug. Some coated mepacrine tablets were relatively insoluble.

The effect of drug treatment on duration of fever symptoms and parasites in the peripheral blood was —

Treatment	Average duration of fever in hours	Average duration of symptoms in hours	Average duration of parasites in hours
No. 1	63.3	64.2	25.5
No. 2	59.7	73.8	40.8
No. 3	75.6	83.8	67.1
No. 4	64.8	71.4	63.0
No. 5	66.0	67.8	48.0

It happened that the patients treated with an initial dose of 0.8 gm. of mepacrine (No. 5) were relatively severe cases with high initial parasite counts while those treated with quinine alone (No. 1) were relatively mild cases. The authors conclude that in the treatment of *P. falciparum* infections in Europeans in West Africa mepacrine alone is as satisfactory as quinine alone or as quinine and mepacrine provided that 0.8 gm. of mepacrine is given during the first 24 hours. Small doses of mepacrine 0.3 gm. daily are capable of dealing with small numbers of parasites in the peripheral blood stream. A low initial parasite count is sometimes followed by a considerable rise in the number of parasites. No toxic effects were noted with the large doses of mepacrine though some of the patients had been taking the drug as a prophylactic, 0.6 gm. weekly for six months or more. In the treatment of uncomplicated cases of malignant tertian fever in Europeans in West Africa—the great majority of cases among people who have been taking a suppressive drug with regularity—quinine can be entirely replaced by mepacrine. Quinine is reserved for cases of cerebral malaria for hyperparasitism (15 per cent. or more of red cells parasitized) for the rare cases where temperatures of 103°–105°F have failed to react to mepacrine and for the still rarer cases in which mepacrine has caused vomiting or psychotic change.

Norman White

NUTRITION REVIEWS. New York. 1944 July v 2, No. 7 207-8. Nutrition and Atabrine Tolerance.

This is a review of recent experimental work on the relationship between the toxic effects of atabrine [mepacrine or atebirin] and the state of nutrition of the experimental animal. It was shown by MARTIN COMBULE and CLARK (*J. Pharm. & Exper. Therap.*, 1939 v 63 156) that atabrine may cause necrosis of the liver and FOSTER and WHIPPLE (*Amer. J. Physiol.*, 1922, v 58 407) found that destruction of liver tissue may cause an increase in the plasma fibrinogen. Experimental investigations of the toxic action of atabrine have recently been made by WRIGHT and LILLY (*this Bulletin*, 1944 v 41 89) by SCUDI and HAMLEN (*ibid.*, 262, 263 & 728) by SCUDI, JELINEK and KUMA (*ibid.* 728) and by HEGSTED, MCKIBBEN and STAKE (*ibid.* 649). Some of the results of this work, mentioned in this review are: (1) the toxic effect of atabrine was greater in starved animals than in well-fed ones. (2) a high-protein low fat diet gave more protection against the toxic action of atabrine than the other diets tested. (3) atabrine in daily doses of 25-30 mgm. per kgm. of body weight did not produce any ill-effects in rats fed on an adequate diet, but larger doses did. (4) atabrine protected rats against the causation of kidney haemorrhages by choline deficiency.

The review concludes with the observation that these investigations offer a clear indication of the interdependence of the nutrition of animals and the action of drugs in the body.

J. F. CORSON.

HAMMICK, D. L. & FRITH, D. Mepacrine Derivatives in Urine. [Correspondence.] *Nature* 1944 Oct 7 461.

Examination by chromatographic methods was made of urine from persons taking mepacrine and a substance was isolated which appears to be 2 hydroxy-6-chloro-9-amino-acridine. This may possibly be the substance designated Fraction C isolated by SCUDI and JELINEK from the urine of dogs dosed with mepacrine (*this Bulletin* 1944 v 41 452). The presence of 2 hydroxy-6-chloro-9-amino-acridine does not interfere with the estimation of mepacrine by MASEN's method (below) or by chromatographic methods. F. HAWKING.

MASEN, J. M. The Determination of Atabrin (Quinacrine Hydrochloride) in Blood and Urine. *J. Biol. Chem.* 1943 v 148 529-39 [Summary taken from *Chem. Abstr.* 1943 Oct. 10 v 37 No 19 5751. Signed H. J. TAGGON.]

The detn. is carried out as follows. Into a 25-ml. separatory funnel add 3 ml. 4N NaOH, 8 ml. iso-PrOH-iso-BuOH mixt. (equal parts), 1 ml. of water, 7 ml. petr. ether, 5 ml. of blood. Mix and shake vigorously for 5 min. Decant, discard the lower layer and decant again after centrifugation. Add 10 ml. 0.3 N NaOH, shake for 1 min. Decant, discard the lower layer and decant again after centrifugation. Add 10 ml. of 30 per cent. iso-PrOH in 0.1 N HCl, shake and decant after 5 min. centrifugation. Draw off 8 ml. of the lower layer, contg. atebirin in a fluorometer cuvette. The blank is the iso-PrOH acid soln. Add 1 ml. NaOH borate buffer mixt. to each cuvette (Na borate 4 g. in 1.35 N NaOH 100 ml.) and read. The control is treated the same way as sample. 1 ml. of water has been replaced by 1 ml. of atebirin base soln. (contg. 0.0025 mg. atebirin). The sensitivity of the method is 0.1 mg. per l. of blood. It is applicable to plasma and urine.

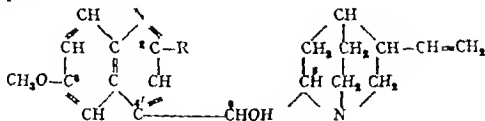
GELLER W. Schädigungen des Zentralnervensystems durch Atebrin? [Does Mepacrine damage the Central Nervous System?] *Deut med Woch* 1944 Mar 3 v 70 No 9/10 123-5

Much of this paper is polemical. KÄHLER (*Deut med. Woch* 1943 v 69 No 35/36) described a patient with benign tertian malaria, treated with mepacrine who suffered from inability to concentrate or to reply to questions in the evening. Kahler considered these symptoms to be due to mepacrine. Geller argues at length that they were probably due to the malaria. Geller has administered 4.0 gm. mepacrine during 2-3 weeks to many patients and has treated many others with smaller amounts, and he has never seen any evidence for the view that mepacrine causes damage to the central nervous system. [Large doses of mepacrine given to uninfected volunteers may cause psychotic symptoms so that there is no doubt that the compound in a sufficiently high concentration does affect the central nervous system. On the other hand the experience of the British and American Services during the present war has shown that psychotic symptoms following mepacrine are rare in actual practice and that they usually disappear completely when the mepacrine is discontinued.]

F. Hawking

MEAD J & KOEPLI J B. The Structure of a New Derivative of Quinine. *J Biol Chem* 1944 Aug v 154 No 3 507-15 2 figs

A crystalline product was recently obtained by KELSEY *et al* [this *Bulletin* 1944 v 41 823] when rabbit liver was allowed to react with quinine *in vitro*. The present investigations were undertaken in order to establish the constitution of the new product referred to by the authors as QDP (quinine-derived product). Evidence has been obtained that it is a simple derivative of quinine in which a hydrogen atom of the parent substance has been replaced by a hydroxyl group as shown in the accompanying formula in which R=H in quinine and R=OH in QDP. [Many substances are known to be eliminated by the animal organism as hydroxy derivatives e.g. benzene benz pyrene phenothiazine to quote only a few.]



The new product is a homogeneous optically active (laevo-rotatory) crystalline substance with M P 247.5-248.5°C. It is soluble in the common organic solvents except hydrocarbons and is insoluble in water. It dissolves in dilute mineral acids but not in ammonia or N alkali hydroxides although soluble in 3N solutions of the latter. It does not appear to have a titratable acid group. All its solutions exhibit a dark blue fluorescence and the dissolved substance is readily adsorbed on a column of calcium carbonate.

The assigned formula was arrived at by the use of chemical and physical methods including a comparison of the absorption spectra of quinine, 2-hydroxy-6-methoxy-4-methylquinoline and QDP. [The maxima and minima of the two latter substances lie close together and the values of wave lengths for these points as given in the text would appear to have been interchanged in the accompanying figure. There also appears to be a discrepancy in the wave length recorded for one minimum in the case of quinine.]

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The new product was shown to be homogeneous and the evidence on which the correctness of the assigned formula is based is supported by the analytical results, by the molecular weight as shown by hydrogenation experiments, and by the presence of an intact quinuclidine ring. Other evidence indicates that it is the quinoline portion of the quinine molecule which has undergone change with the introduction of a hydroxyl group in the position shown. Two experimental observations made by the authors regarding the structure of QDP require further investigation but do not invalidate the formula assigned to it.

J. D. Fulton

Sumner M. L. Exoerythrocytic Stages of *Plasmodium falciparum*. *J. Parasitology* 1944 June v 30 No. 3 177-8.

The malarial parasite discovered in 1941 in a turkey by HERMAN was studied by the author in experimentally inoculated turkeys and ducks. In three of ten turkeys, but in none of fifteen ducks, exoerythrocytic schizonts were found in the brain, lungs, spleen and liver. It is considered that the schizonts described by PURCHAS in 1942 (this Bulletin 1943 v 40 363) as occurring in endothelial cells of small blood vessels of the liver, spleen and brain of infected turkeys may have been the same exoerythrocytic schizonts.

C. M. Wenyon

BLACKWATER FEVER.

MARGRAITH, B. Blackwater Fever Anuria. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1944 Aug. v 38 No. 1 1-17 3 figs. [55 refs.] Discussion 17-23 (HOWARD A. C. HELME, A. C. de B. STANLEY, J. A. MARSON BARR, P. STANNUS, H. S. CHESTERMAN C. C. MARGRAITH (in reply))

Colonel MARGRAITH gives a short review of the more important literature on the mechanism of oliguria and anuria in blackwater fever and on the effects of alkali therapy in that condition together with some observations "a full account of which will be eventually available, on a series of 32 cases of black water fever with renal insufficiency observed in the West African Command 1941 to 1943.

He points out that since 1922 the mortality rate of blackwater fever has increased from 20 per cent. (8,049 cases) to about 25 per cent. (305 cases receiving alkali therapy since 1931). Whether alkali therapy is successful or not in preventing renal failure (the evidence on this point is conflicting and unsatisfactory) a decrease rather than an increase in the total mortality rate might have been expected if it were of practical value, as half the deaths in blackwater fever are associated with anuria.

The rationale of alkali therapy is based on the work of BAKER & DODDS, who showed that insoluble pigment was precipitated from haemoglobin-containing urines if acid and of a high salt content. Thus, they supposed, produced renal failure by mechanical blockage of the tubules. Margraith advances 8 points against this theory —

- 1 The urine in 17 original cases was as frequently alkaline as acid "before the onset of anuria. In a series of 25 patients developing anuria who had acid urine at the onset of blackwater fever" it became alkaline in 7 and it stayed permanently acid in 8. Previous work is cited, illustrating the failure of damaged kidneys to secrete alkaline urine, even when alkali administration is pushed to the point of alkalosis.

2. Nor does the chloride content of the urine in blackwater fever about 0.5 gm per 100 cc. appear from the literature to be sufficiently high to facilitate precipitation of pigment.

3. Haemoglobinuria may occur without anuria even with acid urine and especially in conditions other than blackwater fever.

4. Again in some cases of blackwater fever oliguria and anuria kidney failure develops after the haemoglobinuria has ceased (sometimes many hours later) and may fail to develop after recovery from oliguria although haemoglobinuria may persist.

5. Anuria and oliguria develop in conditions and in circumstances which exactly parallel the renal failure of blackwater fever but in which there is no haemoglobinuria.

6. The degree of blockage found in kidney tubules postmortem was insufficient to account for anuria.

7. If blockage were the primary factor it would be expected that what urine was passed coming as it did from unobstructed nephrons would be normal in its constitution. In fact this is not so. To account for this on the theory of blockage it would be necessary to show that the convoluted tubules have been so damaged by distension that they fail in their function and recover only slowly over a period of weeks. Histological evidence of such distension in the form of dilated capsular spaces and grossly dilated tubules is not a common finding in blackwater fever anuria.

8. Although the urine passed in the immediate post-anuric and recovery phases occasionally contains massive deposits made up of tarry material (WAKEMAN 1929) [this *Bulletin* 1929 v. 23 1015] it is often perfectly clear and relatively free from casts and other debris.

It is argued that the intense alkali dosage now advocated may have a depressing effect in blackwater fever both on kidney function (evidence being adduced from the renal lesion associated with the dehydration and salt depletion of persistent vomiting and alkalosis) and generally (since patients with damaged kidneys are more liable to develop alkalosis). Nevertheless alkaline treatment may be useful for individual cases where acidosis is threatened or has developed or where a mild saline diuretic would be of value. If alkaline therapy is to be used it must be controlled by measurement of plasma CO_2 or by the reaction of the urine after moderate administration say 15 gm. of alkali if the alkali reserve rises fast and the urine reaction does not change then continuation of alkaline treatment is not indicated.

The renal lesion is next considered. A condition resembling shock is seen the blood pressure is usually low in the early stages of anuria [but not in the 5 cases figured] oliguria and nitrogen retention develop with failure to secrete a concentrated urine the changes in the kidney are congestion of the medullary vessels relative 'anaemia' of cortex, including glomeruli degenerative changes in the tubular epithelium especially in the region of the ascending loop of Henle and the distal convoluted tubules the presence of haemoglobin products or haemoglobin-stained casts in the tubules.

This state for which the name tubulo-vascular renal syndrome is suggested is seen in many other conditions such as incompatible transfusion crush syndrome alkalosis septic abortion, concealed accidental haemorrhage cholera, yellow fever sulphonamide haemoglobinuria mercurial and bismuth poisoning and has been exactly reproduced in rabbits by lithium urate and in rats by acid sodium phosphate.

Some suggestions are given for the probable mechanism of the renal lesion [as detailed in abstract of the paper by MAEGRAITH & FINDLAY below] together with some possibly fruitful lines of research.

In the discussion Dr A. C. HOWARD Dr A. C. de B HELME Dr H S STAMNUS and Dr C. C. CHESTERMAN spoke. Brigadier SINTON suggested that the altered distribution of renal blood flow might be caused by pressure on arteries due to swelling of the tubular epithelium. He advocated that before alkali therapy be condemned entirely a controlled series of trials by the alternative case method should be made as Colonel Macgraith had suggested.

In reply to a question by Sir Philip MARSON BARR about blood transfusion, Colonel Macgraith stated that this was "a common factor in many of the West African cases" but that they had refrained from using it until the oxygen carrying power had fallen to a dangerous level.

E G L. Bywaters

MACGRAITH B. G. & HAVARD R. E. Dangers of Intensive Alkali Treatment in Blackwater Fever. *Lancet* 1944 Sept. 9 338-9 [42 refs.]

This is a summary of data and arguments which are detailed at slightly greater length in the paper by MACGRAITH abstracted above.

E G L. Bywaters

MACGRAITH B. G. & FINDLAY G. M. Oliguria in Blackwater Fever. *Lancet* 1944 Sept. 23 403-4 [19 refs.]

The views expressed in this paper are based on the study of 35 cases of blackwater fever with renal insufficiency observed in the West Africa Command 1941-1943. The arguments regarding therapy have been given rather more fully in the paper by MACGRAITH abstracted above.

The blockage of the renal tubules with debris and haemoglobin products is not the deciding factor in the production of oliguria. Observation of the reactions of the skin to stroking (failure in severe cases to develop almost any skin vascular responses) and of the hepatic vessels at autopsy (centrilobular congestion and necrosis) suggest that peripheral vascular atonic collapse with subsequent redistribution of intrarenal blood-flow and depression of glomerular filtration may play a part in the production of oliguria.

The changes found in the renal epithelium are thought to be partly due to anoxia.

E G L. Bywaters

CALEWAERT D. Pathogène et traitement de l'hémogloburémie des pays chauds. [The Pathogenesis and Treatment of Blackwater Fever]. *Rec Trav. Soc. Méd. Congo Belge* Léopoldville 1944 Jan No 2, 151-6. [14 refs.]

The author rejects the view that acidosis is one of the causes of the haemoglobinuria of blackwater fever since it is so often present in people who have not haemoglobinuria. His view is that the intravascular haemolysis is due to lowered tension of the blood. He has measured the surface tension of the blood in normal persons and in patients with blackwater fever by means of the apparatus of Lecomte du Noury [interfacial tensiometer] and distinguishes two measurements: (a) relative dynamic surface tension (a rough approximation) these were respectively 57-58 dynes/cm. and 58 dynes/cm. in blackwater fever the corresponding figures were 50-52 dynes/cm. and 45-50 dynes/cm. This lowered tension produces haemolysis. It has been found that the addition of a trace of soap to an isotonic solution of sodium chloride containing red blood corpuscles produces haemolysis and the author thinks that malaria parasites have an identical action by communicating their low surface tension to the red cells. Certain apparently related observations are mentioned in support of this theory: the surface tension of the blood is relatively low in young people and they are particularly prone to get haemoglobinuria. haemoglobinuria is

associated with fever and in fever of any kind the surface tension of the blood is lowered quinine hydrochloride (but not sulphate or formate) lowers the tension

Treatment should be in accordance with this view on the first day three injections of 150-200 cc of 3 per cent. sodium bicarbonate in glucose saline iv and 3-4 injections of 0.05 gm. of ephedrine hydrochloride (or ephedrine) subcutaneously on the second day two injections of sodium bicarbonate and 2-3 injections of ephedrine on the following days the treatment is adjusted according to the symptoms. In mild cases with the urine more or less alkaline sodium bicarbonate is given by mouth.

The author claims that the moment when the urine will become clear can be predicted by measuring the surface tension of the blood.

Both ephedrine and sodium bicarbonate are necessary the suspension of either is apt to cause a return of the haemoglobinuria.

In very severe cases blood transfusion is indicated.

J F Corson

TRY PANOSOMIASIS

- i. MACKICHAN I W. Rhodesian Sleeping Sickness in Eastern Uganda. *Trans Roy Soc Trop Med & Hyg* 1944 Aug 1 38 No. 1 49-60 1 map
- ii. DUKE H L. Rhodesian Sleeping Sickness. [Correspondence.] *Ibid* Nov. 4 38 No 2 163-5

i. This is an account of an outbreak of Rhodesian sleeping sickness in the Uganda Protectorate which appears to have begun in November 1940 up to the middle of 1943 there had been 2 432 cases and 274 deaths. The early cases seem to have been infected near Jinja and afterwards the disease appears to have spread eastwards to beyond the Kenya border. The peak of the epidemic was reached in March 1942, when over 100 new cases a month were seen and over 1 000 were under treatment afterwards the number of new cases decreased and at the time of writing they averaged 10 to 20 a month.

Clinically the disease resembled Rhodesian sleeping sickness but laboratory animals were not inoculated until December 1941 it was then found that the trypanosome was *T. rhodesiense*. The author states that this is apparently the first time that *T. rhodesiense* has been isolated in Uganda.

Three species of *Glossina* are found in the area—*G. pallidipes*, *G. palpalis fuscipes* and *G. brevipalpis* the last species exists in very small numbers. The distribution of these flies has been investigated and CHORLEY has shown that *G. palpalis fuscipes* breeds in the evergreen forest as far as 10 miles from permanent water within the 50-inch rainfall contour. The distribution of *G. pallidipes* somewhat overlaps that of *G. palpalis fuscipes*. The author thinks that the evidence points to *G. pallidipes* as the most important if not the only vector of *T. rhodesiense* in this outbreak. Rats were infected with polymorphic trypanosomes by wild *G. pallidipes* and the blood of one of them infected a volunteer. The flies were caught and fed on the rats by C. H. N. JACKSON of the Tsetse Research Department Tanganyika Territory about 3,500 flies fed on 50 rats and 5 of the rats became infected with polymorphic trypanosomes. Their blood was injected into five volunteers, four of whom showed no reaction up to the 10th day when they were given a course of antrypol the fifth man developed a painful swelling at the site of the injection on the 4th day his temperature rose to 102°F on the 5th day and trypanosomes were found in his blood on the 6th day. He was then treated with antrypol. [Subinoculation

[January 1945]

of animals from this volunteer is not mentioned but it is almost certain that he was infected with *T. rhodesiensis* and not *T. gambiense*. The author states that *T. brucei* was found some years ago in a dog at Kiterera in this area, and, more recently some dogs at Jinja have been found infected. Two rats were infected with polymorphic trypanosomes by *G. palpalis fuscipes* caught in the Kiterera area and the blood of one was inoculated into a volunteer but failed to infect him. Other rats were infected with polymorphic trypanosomes by *G. palpalis fuscipes* caught in Buruma Island. One strain was sent to Tinde, Tanganyika Territory but failed to infect volunteers there.

As regards the origin of the epidemic the author thinks that the infection was introduced into Uganda by labourers coming from Tanganyika Territory west of Lake Victoria.

11. The author [this Bulletin 1917 v 9 31] found heavy salivary gland infections in 3 per cent. of 65 wild *Glossina pallidipes* caught on the escarpment above Lake Albert. This is an unusually high gland infection with polymorphic trypanosomes of the type of any species.

He also points out that *Trypanosoma rhodesiensis* was found in Uganda several years ago [see DICKS this Bulletin 1931 v 23 346 1933 v 30 433 1934 v 31 566] J F Corson.

WILLIAMS, W. L. On the Activity of the Tsetse, *Glossina pallidipes* and other Tsetse during a 24 Hour Period. *Rhodesian Agric. J.* 1943 v 40 No. 6 368-70. [Summary taken from *Rev. Applied Entom.* Ser. B 1944 Sept. v 32, Pt. 9 162.]

On 28th-29th October 1943 continuous patrols, each of two hours duration were made over a period of 24 hours with a donkey near a pontoon across the Busi River in Portuguese East Africa about seven miles from the Southern Rhodesian border with the object of determining the diurnal and nocturnal activity of *Glossina pallidipes* Aust. and comparing the findings with those of Vanderplank in Tanganyika and Chorley and Hopkins in Uganda. It was also intended to make incidental observations on the activity of *G. brevipalpis* Newst. and *G. morsitans* Westw. Only flies that alighted on the donkey were caught. The night was moonless. The fact that the largest catch was made in the last hour showed that the killing of tsetse during the patrol had little effect on the local population. In all, 42 males and 16 females of *G. pallidipes* were taken, nearly all between 5 and 6 a.m. and 5 and 6.20 p.m. South African Standard Time. Large numbers of *G. brevipalpis* about 99 per cent. of which were males were observed on the road between 5.48 and 6.30 p.m. and 5 and 6 a.m. but they were not greatly attracted to the donkey. Only two individuals of *G. morsitans* were seen, and these were the only tsetse flies taken between 10 a.m. and 5 p.m. Air temperatures during the hottest part of the day inhibited activity but the night temperature was never low enough to do so.

JACK, R. W. The Life Economy of a Tsetse Fly [exemplified by *Glossina morsitans* Westw., in S. Rhodesia]. *Rhodesian Agric. J.* 1944 v 41 No. 1 25-38.

FADY, A. La ponction sternale comme moyen de diagnostic à la période nerveuse de la maladie du sommeil à *T. gambiense*. [Sternal Puncture as a Means of Diagnosis of the Nervous Stage of Gambian Sleeping Sickness.] *Rec. Trav. Soc. Méd. Congo Bdg. Léopoldville.* 1944 Jan., No. 2, 127-9

Sternal puncture was performed in 20 sleeping sickness patients in the Belgian Congo. clinically the disease was in an advanced stage and this was confirmed by lumbar puncture. Eight of the patients had been given Bayer 205 [Germanin]

prophylactically from 2 to 9 months before but it is thought that they were already infected when they received the prophylactic injections. In all cases no trypanosomes were seen on repeated examination of the blood and (except one) gland juice but trypanosomes were found by sternal puncture in 11 of the 20 patients in numbers varying from 1 to 46 the higher numbers being found in children. It is concluded that this method is useful and justifiable in such cases to confirm the diagnosis [See also this *Bulletin* 1938 v 35 704 1939 v 36 216 and 217 1940 v 37 402 1941 v 38 304 and 1944 v 41 14]

J F Corson

SEYRO NIETO L. Contribución al diagnóstico por el laboratorio de la tripanosomiasis humana. [Laboratory Diagnosis of Human Trypanosomiasis] *Med Colonial* Madrid. 1944 June 1 v 3 No 6 373-92, 3 charts [22 refs.]

During a campaign against Gambian sleeping sickness in Santa Isabel Fernando Po the author made observations on the blood and cerebrospinal fluid which he thinks may assist in the diagnosis often difficult of the disease.

The blood picture—Hyperleucocytosis [above 8 000 per cmm] was present in 50 per cent. leucopenia in 34 per cent. and a normal count in 16 per cent. There was usually lymphocytopenia. An interesting observation was that the number of eosinophils was below the normal in 83 per cent. of patients although filariasis and various intestinal worm infestations were very common. The average number of blood platelets in normal natives was found to be 230 000 per cmm while in sleeping sickness it varied from 300 000 to 370 000

The coagulation time—The average normal time was 6.5 minutes in sleeping sickness it was 4.5 minutes.

The serum calcium.—In normal natives the average content was 10.5 mgrm. per 100 cc. in sleeping sickness it was 9.12 mgrm

The cerebrospinal fluid—The author used Sicard's method for the total protein Nonne-Apelt, Pandey and Welchbrodt tests for globulin and Lange's colloidal gold reaction and counted the cells in a Fuchs-Rosenthal counting chamber. He agrees with ZACHUCKE [this *Bulletin* 1933 v 30 432] that the total protein estimation is less valuable than the tests for globulin and especially than the colloidal gold test. With a constant total protein he has found marked changes to occur in the globulin reactions. He also considers the cell count more useful than the total protein figure but with a normal cell count and normal total protein there may be an abnormal gold curve—he accepts the colloidal reaction in such a case as indicating a pathological fluid and found that this reaction gave the only indication of involvement of the central nervous system in 27 per cent. of cases [See also FAIRBAIRN this *Bulletin* 1934 v 31 559]

J F Corson

EAGLE H HOGAN R. B DOAK G. O & STEINMAN H. G. The Therapeutic Efficacy of Phenyl Arsenoxides in Mouse and Rabbit Trypanosomiasis (*Tryp equiperdum*) *Pub Health Rep* Wash. 1944 June 16 v 59 No 24 765-83 3 figs [14 refs.]

This paper describes a continuation of studies on the phenylarsenoxides. Previous papers (EAGLE HOGAN DOAK and STEINMAN) *J Pharm & Exper Therap* 1940 v 70 221 *ibid* 1942 v 74 210 had dealt with their toxicity and spirochaetocidal action. In the present work 54 phenylarsenoxides were assayed for their trypanocidal action *in vitro* upon *T. equiperdum* these tests were made at room temperature (23°C.) allowing a period of 2-4 hours incubation before the result was read [The technique described by YORKE and MURGATROYD (this *Bulletin* 1931 v 28 350) might have yielded results which

corresponded more closely to what happens *in vivo*] Twenty-six compounds were studied for their toxicity and trypanocidal action in mice and four were studied in rabbits. [Curative action of the compounds was judged by survival of the mice for 30 days rather than by examination of the blood for trypanosomes—some of the mice may have died from other causes.] Various phenyl arsenic acids were also examined.

Although there was a rough correlation between the trypanocidal and spirochaetocidal activity of phenyl arsenoxides the two assays were sometimes wholly discrepant. There was a sufficiently close correlation between the trypanocidal activity *in vitro* and *in vivo* to justify the use of the former as a screening procedure with respect to therapeutic activity upon spirochaetes. Weakly active compounds were however usually more effectively trypanocidal *in vivo* than would have been expected from their direct action *in vitro*.

Phenyl arsenoxides regularly gave a more favourable chemotherapeutic index in the treatment of mouse trypanosomiasis than the corresponding arsenic acids. The chemotherapeutic index (LD₅₀/CD₅₀) of nine arsenic acids varied between 1.4 and 9 to be compared with indices of 3.5 to 28 for the corresponding arsenoxides. In the treatment of rabbit trypanosomiasis, the difference was not so marked, but was again in favour of phenyl arsenoxides.

Various types of substituents have had fairly regular effects on the trypanocidal activity toxicity and thus on the chemotherapeutic index of phenyl arsenoxide.

(a) Nitro (NO₂) chloro (Cl) methyl (CH₃) amino (NH₂) and hydroxyl (OH) groups had no significant effect on the activity toxicity ratio.

(b) Acidic groups (COOH or SO₃H) usually caused a striking decrease in trypanocidal action.

(c) Amide-substituted compounds (—CONH₂) or those with a substituent containing a terminal acetamide (—CH₂CONH₂) group were uniformly low in toxicity and usually had a favourable activity toxicity ratio varying up to 7.4 times that of the unsubstituted compound. In the treatment of mouse trypanosomiasis the chemotherapeutic index (LD₅₀/CD₅₀) of such compounds varied between 2.8 and 28.3 the corresponding index for the unsubstituted phenyl arsenoxide being less than 1.

(d) Substitution of an amide hydrogen with —CH₃ or —C₂H₅ (e.g. —CONHCH₃) reacted unfavourably on the activity toxicity ratio of the compound but similar substitution with a group containing a terminal hydroxyl, acetamide or nitrile (—CH₂CN) linkage did not adversely affect the favourable effect of the amide group.

The most promising compound of the present series was *p*-butyric acid derivative of phenyl arsenoxide OAsC₆H₄CH₂CH₂CH₂COOH. This compound was an exception to the rule that acidic substituents (e.g. —COOH) inhibited trypanocidal activity and its activity *in vitro* was about half that of phenyl arsenoxide. The LD₅₀ value in mice on single intraperitoneal injection was 33.4 per kgm. the CD₅₀ value in that species was 1.8 mgm./kgm. and the LD₅₀/CD₅₀ ratio of 20.5 was the third highest in the entire series. In rabbit trypanosomiasis treated by four consecutive daily injections the LD₅₀ value was 16 mgm. per kgm. the CD₅₀ was 3.6 mgm./kgm. and the LD₅₀/CD₅₀ index was 4.4 the highest of all the compounds tested. The favourable chemotherapeutic index of this compound is due to its unusually high trypanocidal activity (for this type of compound) without undue toxicity.

This compound is also said to be effective against strains of trypanosomes resistant to most other arsenicals. [This paper describes a very extensive investigation into the relation between chemical structure and trypanocidal action and it should be studied in the original by all those interested in this subject.]

F. Hesketh

LUIZ DAO L. La punción esplénica como medio de diagnóstico en un caso de enfermedad de Chagas. [Spleen-Puncture in Diagnosis of Chagas's Disease] *Bol Hospitales Caracas* 1944, Jan-Feb v 43 No 1 10-17 1 fig

The patient an agricultural worker of 40 years had been living for some years in places where chepitos [a local name for Reduviid bugs] were abundant. He had been having fever of a low type unaccompanied by shivering or sweating for about three years and he complained of great weakness. During recent months however the fever was more acute with both shivering and sweats. On coming under the author's observation he was seen to be pale and anaemic and to have some swelling of the face. His spleen was much enlarged and the liver extended to two fingers breadths below the costal margin. His blood contained 2 624,000 red cells and 2,200 white per cmm haemoglobin 45 per cent. colour index 0.8. Polymorphonuclears were 34 per cent. lymphocytes 36 large mononuclears 20 eosinophiles 8 and basophiles 2 per cent. Kahn gave a 3 plus (there were indications of old venereal disease). *P. vivax* was seen in smears but no trypanosomes the faeces showed ova of *Necator*. Venodiagnosis was undertaken and later proved positive for *T. cruzi* in the meantime spleen puncture was performed and trypanosomes and gametes of *P. vivax* were seen. The patient was thus found to be suffering from syphilis malaria Chagas's disease and ankylostomiasis.

Spleen puncture is therefore a useful measure for diagnosis of Chagas's disease and is doubly useful in a country where kala azar also occurs

H Harold Scott

ZAMBRA E. R. La enfermedad de Chagas su historia. Estudio de la enfermedad de Chagas en el Norte Santafesino (R Argentina) El signo o Signal de Romafia. [Chagas's Disease Its History A Study of the Disease in Northern Santa Fé (Argentine Republic) Romafia's Sign.] 95 pp 9 figs. 1944 Buenos Aires

The first part of this booklet giving the history of American trypanosomiasis from the time of its being first brought to notice by Carlos Chagas in 1909 in the State of Minas Geraes is good. The author relates with full documentary evidence in support how the range of its existence was observed to become wider and wider and how more and more reservoir hosts and transmitters were discovered—all most interesting but not new to diligent readers of good modern text-books on tropical medicine or of this *Bulletin*. The remainder of the booklet in the opinion of the reviewer at least serves little useful purpose. Though amply documented the extracts and the comments upon them are purely polemical and a good deal of it little else than eulogy and fulsome flattery of Professor Salvador Mazza and abuse of Dr Romafia.

H Harold Scott

LEISHMANIASIS

BURKE E & CHAKRAVARTY K. C. A Preliminary Note on the Treatment of 21 Cases of Kala-Azar with Sodium Antimony Gluconate (with special reference to its Suitability for Mass Administration on Tea Estates) *Indian Med Gaz* 1944 June v 79 No 6 268-71 7 figs.

The authors who have had considerable experience of kala azar in Assam tea gardens give an account of their treatment of 21 cases of this disease with sodium antimony gluconate (stibatin of Glaxo Laboratories). The product was

supplied in rubber-capped bottles each containing 30 cc. of a clear sterile liquid, each cc. of which contains 20 mgm. of pentavalent antimony. Various doses were tried both intravenously and intramuscularly till, finally it was decided that a daily dose of 1 cc. could be given for each year of age. Above 15 years of age the dose was limited to 15 cc. though the view is expressed that 20 cc. daily could with safety be administered. The full course recommended by the makers is 60 cc. but the authors have given as much as 100 cc. in 7 days. In young children the injections were made intramuscularly. They are quite painless and therapeutically as effective as the intravenous injections which are also free from unpleasant reactions. A cure was obtained in all the 21 cases a result which leads the authors to remark that they believe the drug to be as good as if not superior to any other antimonial kala azar remedies.

C. V. HENSON

KIRK, R. & HENRY, A. J. Observations on the Toxicity of Stilbamidine. *Ann Trop Med & Parasit* 1944 Sept 30 v 38 No. 2, 99-118. [30 refs.]

In 1909 and 1910 44 cases of kala azar in the Sudan were treated successfully with stilbamidine. Large stocks of stilbamidine were laid in and were used during the subsequent period when communication with Britain was difficult but the clinical results gradually became less satisfactory owing to the increasing frequency of toxic reactions and to the incompleteness of the response to therapy.

The immediate reactions recognized as occurring after the intravenous injection of the aromatic diamidine compounds include a severe transient fall of blood pressure, formication, sweating, breathlessness, vomiting etc. all of which pass off in a few minutes. In some cases thrombosis of the veins at the site of injection occurred. But after a time in the Sudan, other toxic effects began to be observed. These effects did not develop until 1-3 months after the completion of treatment and there were two main types.

(1) *Nervous sequelae*—(a) Paraesthesia, anaesthesia, formication, and hyperaesthesia over the distribution of the trigeminal nerve and sometimes swelling of the face. (b) Peripheral neuritis of the legs and foot-drop. (c) In rare cases epilepsy or mania.

(2) *Fatal delayed poisoning*—The patient who had previously been well was suddenly attacked by nausea and vomiting, passed into coma and died in 1-4 days.

The storage and excretion of the compound were studied by means of the method described by HENRY and GRINDLEY [this *Bulletin* 1943 v 40 122] to estimate the drug in the excretions. Owing to the difficult conditions under which the investigations were made the data obtained were less complete than was desired. However it was shown that stilbamidine tends to be rapidly absorbed by the tissues and that it is released only slowly for excretion. Two patients were given nine doses of 50 mgm. (1 mgm. per kilo) intravenously on alternate days and the urine was examined. During the period corresponding to the first three doses only about 15 per cent. of the dose was excreted in the urine, then the excretion increased and by the 7th or 8th dose about 80 per cent. of the last dose was excreted, within one day after the last dose 200 mgm. had been excreted out of a total dosage of 450 mgm. Fifteen minutes after the ninth dose the concentration in the plasma was about 0.7 mgm. per 100 cc. and five days later none could be detected in the plasma (<0.125 mgm.). A few hours after the ninth dose the cerebrospinal fluid, perspiration and sputum contained no detectable drug. The absence of the drug from the spinal fluid indicates that it is not likely to be effective against trypanosomiasis of the central nervous system. Five days after the last dose the urine contained

only traces of the drug and these were still present after 25 days. [The absorption and excretion of stilbamidine resemble those of mepacrine in many ways. Mepacrine is another basic substance which tends gradually to accumulate in the tissues during the daily administration of small doses and which is slowly liberated (in part) for excretion in the urine.]

The above investigations on the excretion of stilbamidine were discontinued because evidence accumulated that the toxic symptoms were due to chemical changes in the drug. Thus one series of 14 cases was treated with solutions freshly prepared on each occasion. 7 were cured, 4 were lost to sight and 3 died probably from kala azar without any suspicion of poisoning. Another series of 18 cases was treated with a solution 1-4 weeks old (exposure to light unknown). 3 were cured, 5 were observed only for 1½-4 months and 10 died, many of them with the late toxic symptoms described above. Work by FULTON and YORKE [this *Bulletin* 1943 v 40 23] showed that solutions of stilbamidine become more toxic to mice on exposure to light—this finding was confirmed in Khartoum. Chemical changes appear to take place especially at the double bond of the stilbene radicle but their exact nature is still uncertain. In mice and rabbits poisoned by these solutions which had deteriorated there was much tubular nephritis and the livers showed congestion with blood and fatty degeneration. Opportunities to obtain tissue by autopsies of the human cases of poisoning were very limited. Evidence of renal and hepatic injury was found in a limited number of specimens but its significance was uncertain.

It is concluded that the serious toxic effects which had been observed were due mostly to the early chemical changes which occur in stilbamidine when solutions are exposed to light. [This is an important paper which should be studied in the original by all interested in this subject.] F Hawking

FULTON J D The Therapeutic Action of some Newer Aromatic Diamidines on *Leishmania donovani* Infections of Golden Hamsters (*Cricetus auratus*). *Ann Trop Med & Parasit* 1944 Sept 30 v 38 No 2 147-68 [22 refs.]

Hamsters were infected with leishmania isolated from an Indian case of kala azar in 1939. Six weeks later a portion of the spleen was sampled and treatment commenced a week later. It was found that ten doses of 20 mgm. per kilo of stilbamidine given in solution by intraperitoneal injection three times a week cured 13 out of 15 animals. [Stilbamidine is 4,4'-diamidinostilbene—the maximum tolerated dose in mice is 1.0 mgm. per 20 gm.] 4,4'-Diamidino-2-hydroxy-stilbene (max. tol. dose in mice 1.0 mgm.) is equally effective therapeutically i.e. 20 mgm. ten times cured practically all the animals. The monomethyl and dimethyl derivatives of stilbamidine are also curative but they are not so effective as stilbamidine against leishmaniasis although very effective against *Trypanosoma congolense* in mice. 4,4'-diamidino tolane and 4,4'-diamidino diphenyl urea showed little activity while the corresponding diphenyl sulphone and diphenyl hexane derivatives failed to influence the course of the infection. F Hawking

BALL D & RYAN R. C. Cutaneous Leishmaniasis. *Bull U.S. Army Med Dept.* 1944 Aug No 79 65-73 1 fig

The paper gives an account of 499 proved cases of cutaneous leishmaniasis in American forces in the Middle East. The exact locality is not mentioned—it was presumably in Persia or the near vicinity as it took ten days for troops to reach it from India, while one of the authors made a trip to Bagdad, where he observed that the scars left by treated sores in that city were more conspicuous

than those following cure in the present series of cases. Of the 499 cases, 102 were transferred to other stations before treatment, leaving 397 under observation. These had a total of 1 768 lesions the average number per case being 4.3. The minimum number of lesions was one and the maximum 29. The majority of patients were treated and cured by intravenous injections of neostam [Burroughs Wellcome & Co.] given twice a week. The first three doses were of 0.05 0.1 and 0.15 gm. subsequent ones being of 0.2 gm. except in a few cases which reacted unfavourably when the dose of 0.15 gm. was not exceeded. The total quantity given to each patient averaged 1.14 gm. Toxic reactions which usually appeared in from 45 to 90 minutes, consisted of mild nausea, severe projectile vomiting diarrhoea and, in three cases collapse. These reactions were quickly rebuffed by giving morphine 0.011 gm. [1/8 grain] hypodermically. When the maximum dose of neostam was reduced to 0.15 gm. given at noon, the mid-day meal being withheld, the reactions were reduced to 0.83 per cent in the last 850 injections. The unpleasant taste following the injections was prevented by chewing gum. Of 221 cases treated by intravenous neostam 208 were cured 14 being still under treatment at the time of writing. The minimum time for cure was two weeks and the maximum 20 weeks—an average of 14.5 weeks. There were no failures. Of 138 cases treated by infiltrating a sore with 1 cc. of a 1 per cent. berberine sulphate solution 31.8 per cent. were failures. Ethyl chloride spraying was successful in curing a few very early cases. X-ray therapy was tried in a few patients of 10 who were followed, 6 were cured—the one failure was subsequently cured by neostam. The conclusion is that neostam is effective in the treatment of cutaneous leishmaniasis. Other methods of treatment are less satisfactory though effective in certain cases.

C. M. HAYSON

BELTRÁN E. & R. LARENAS M. Acción de algunas sulfamidas sobre *Leishmania brasiliensis* en cultivo y sus contaminaciones bacterianas. [Action of certain Sulphonamides on *L. brasiliensis* Cultures and their Bacterial Contaminations.] *Rev. Inst. Salubridad y Enfermedades Trop. Mexico* 1944 Mar v 5 No 1 53-7 English summary

The authors have tested the action of sulphamidamide sulphapyridine and isidiazine on cultures of *Leishmania brasiliensis*. They have found that in a concentration of 1/1 000 these substances were without lethal action on the flagellate forms of leishmania though in a concentration of 1/100 they are lethal. It was thought that in a concentration of 1/1 000 they might be used to get rid of bacterial contaminations in cultures of leishmania but they were not lethal to the bacteria. The authors admit that it is impossible to draw any conclusions regarding the possible therapeutic value of the drugs tried.

C. M. HAYSON

FEVERS OF THE TYPHUS GROUP

ANDREWS C. H. KING H. VAN DEN ENDE M. & WALKER, J. Substances chemotherapeutically active against Typhus Rickettsiae. *Lancet* 1944 June 17 777-81

[This very important paper should be closely studied by all who are interested in the chemotherapy of the rickettsial and virus diseases. In a summary it is impossible to do justice to the remarkable investigation described by the authors. The paper itself is a condensed report of a very extensive and highly skilled,

not to say dangerous series of experiments and although these have not yet resulted in the discovery of a cure for the typhus fevers they justify hopes that the authors may be blazing the trail for far reaching developments in this connexion]

In the course of tests of a series of compounds for activity against viruses and rickettsiae it was found that V 147 (*p*-sulphanidobenzamidine hydrochloride) had a definite action in mice infected with typhus rickettsiae. The compound is not a sulphonamide in the popular sense of the term and its action was found to be quite different from that of the sulphonamide group. Most of the work was done with the Wilmington strain of murine rickettsiae but Tunisian and Breuil epidemic strains were used to confirm the results obtained.

Suspensions of the strains were prepared from the lungs of mice which had been inoculated intranasally with infective material obtained by repeated lung passages through mice. The methods are fully described. During and for about an hour after the intranasal injections the mice were kept in the inoculation box devised by van den Ende in this way the risk of droplet infection was greatly diminished so that only one attack of typhus fever occurred among 9 non immune persons who inoculated several thousands of mice over a period of 18 months whereas before the use of the box all the 5 persons engaged in the same work had been attacked within a month of commencing the inoculations.

By experiments, it was found possible to arrive at a strength of the infecting suspension which caused the formation of visible dark-grey discrete foci on the surface of the lungs of the infected mice after seven days. The number of the foci gave a quantitative indication of the intensity of the reaction in the animals provided that careful control was exercised over the administration of the anaesthetic. In one series of 14 mice inoculated with the same dilution of the suspension the number of foci ranged from 85 to 135. The concentrated stock suspension retains its full infectivity for at least 4 months when kept at -77°C .

In one group of 5 mice treated by 6 intraperitoneal injections of 4 mgm. each of V 147—the drug being started two hours before inoculation and administered twice daily—no foci were found whereas control mice inoculated in the same way developed numerous foci.

By using different dilutions of the infecting suspension and different doses of the drug it was found that striking benefit resulted from the treatment. Appreciable benefit resulted when the administration of the drug was started after the infecting inoculation—even up to 42 hours after this inoculation.

Another drug, V 186 (*p*-sulphanidobenzamidoxime hydrochloride) which is very closely related to V 147 was equally effective and in some respects was found to be preferable. Ten other drugs differing slightly in their molecular structure from the above were also effective but their suppressive doses approached more nearly to the maximum tolerated doses so that they were less satisfactory.

No less than 154 other drugs were tested but although 84 of these were rather closely related to V 147 and V 186 all were found inactive in the maximum tolerated doses. It was therefore evident that any considerable change in the molecular structure led to a loss of the strictly specific anti typhus properties of the effective drugs.

Further study is being made of the association between the structure of the compounds and their therapeutic power and it is hoped that this will lead to clearer knowledge of their mode of action.

V 186 was also effective when given mixed with the food and when given subcutaneously but V 147 was slightly less effective when given in the former way.

The drugs did not completely destroy the rickettsiae, as was shown by the fact that suspensions of the lungs of the treated mice were still infective though very much less so than suspensions made from untreated mice.

The drugs were ineffective in the treatment of typhus-infected guinea-pigs.

Clinical trials carried out in North Africa and Naples have yielded very disappointing results there was great difficulty in providing that the treatment should be started within the first few days after the onset of the attack, and the drugs for unexplained reasons were toxic for occasional patients.

John W D Meigs

VÍKES IBARROLA, D J Tifus exantemático. Influencia del medio en su difusión. El complejo sanitario y el complejo social. [Exanthematic Typhus. The Influence of Environment on its Spread. The Sanitary and Social Complexes.] *Rev. Sanidad e Hig. Pública* Madrid. 1944 Jan.-Feb v 18 No. 1 1-23, 1 map.

The author discusses 28 outbreaks of typhus fever in which altogether 113 persons were attacked in the Provinces of Zaragoza and Navarra during the years 1841-1943.

The paper deals chiefly with the special problems that arose in connexion with the campaign against the disease in the above two areas. Different methods of control were called for in rural as contrasted with urban regions and also in persons of high social status as compared with the poorer classes of the community. So many factors had to be taken into account that the selection of the most suitable plan of action made great demands on the versatility and tact of the officers of health. The relations between these officers and the private practitioners do not always seem to have been happy, especially in the large towns.

The Weil-Felix test was found invaluable in diagnosis: it was persistently negative in only one case but negative or weak reactions in the early stages of the illness were often wrongly interpreted by inexperienced practitioners who were liable to regard these as excluding the diagnosis of typhus fever.

Early diagnosis or at least suspicion of the disease is stressed as being essential to success in preventing the spread of infection.

John W D Meigs

DING E. Beitrag zur Frage der Tröpfcheninfektion bei Fleckfieber. [Note on the Question of Droplet Infection in Typhus Fever.] *Ztschr. f. Hyg. u. Infektionskr.* 1944 Mar 23 v 125 No. 5 431-6. [25 refs.]

From 76 patients with confirmed typhus fever smears were made daily of material obtained from scrapings of the mucosa of the nose and throat and from sputum and aspirated salivary gland juice. Altogether about 13,000 specimens were made and stained by the methods of Castellada, Machiavello, Grams and Gracian. No rickettsiae could be detected after a thorough search of this extensive material.

Sputum and salivary secretion from patients who had catarrhal manifestations were injected intraperitoneally into 149 guinea-pigs with completely negative results.

Scrapings from the tracheal mucosa of 8 persons, who had died of the disease 2-8 hours previously were made and inoculated into 16 guinea-pigs, with equally negative results.

The possibility of symptomless infection of the guinea-pigs was excluded by attempts to make sub-passages with brain substance.

From the negative results the author concludes that transmission of infection from man to man by droplet infection cannot occur.

John W D Meigs

EYER H & RUSKA H Ueber den Feinbau der Fleckfieber Rickettsiae [The Minute Structure of Typhus Rickettsiae] *Ztschr f Hyg u Infektionskr* 1944 Mar 23 v 125 No 5 483-92 10 figs [12 refs]

This paper is illustrated by 10 photographs made with the electron microscope and reproduced at magnifications of 25 000 diameters

The features of the rickettsiae are very similar to those shown in the illustrations contained in the paper by PLOTZ and his collaborators [this *Bulletin* 1943 v 40 635] and in the paper by WEISS [this *Bulletin* 1944 v 41 378]

The authors have arrived at the same conclusion as Plotz and his colleagues that the rickettsiae approach closely to bacteria in their structural features.

The material was obtained from the intestines of infected lice and although it is stated that *Rickettsia prowazeki*, *R. quintana*, and *R. pediculi* were examined no mention is made of any differences in their appearance

Great variations in shape and size of the organisms are shown in the photographs but in the specimens examined the most numerous forms were of the bacilliform type ('pölstäbe') with a rounded dark shadow at each end of the organism suggesting an analogy with nuclei and called by the author 'nucleoides'. Some of the bacilliform organisms tended to be barrel-shaped. Next in order of frequency came rounded forms most of which contained a nucleoid. There were a few smaller dark round forms which were regarded as nucleoides. Indications of cell division were seen in some of the bacilliform bodies

One of the photographs shows a paratyphoid bacillus which apart from its much larger size is strikingly similar to a bacilliform rickettsia.

John W D Megaw

GALLARDO E SANZ J & PEREZ GALLARDO F Datos experimentales sobre el cultivo de la Rickettsia Prowazeki en la membrana vitelina del embrión de pollo [Experiences in the Cultivation of *R. prowazeki* in the Vitelline Membrane of Chick Embryos.] *Rev Sanidad e Hig Pública* Madrid. 1944 July v 18 No 4 269-73

The authors describe the results obtained in the preparation of typhus vaccine by Cox's yolk-sac method. They began the work under the guidance of Dr SNYDER of the Rockefeller Foundation.

Three strains of rickettsiae from Madrid, Barcelona and Murcia were used. The starting material was a suspension of the brain of an infected guinea pig. The best results were obtained by killing the animals on the 1st or 2nd day of the fever. No difficulty was found in adapting the rickettsiae to vitelline-membrane cultivation. The eggs were used 5-7 days after inoculation. Incubation was at 37°C.

During a period of one and a half years 10,887 eggs were used of these 4,316 died before the 5th day and 451 were found contaminated.

More than 60 litres of vaccine were prepared—enough for 20 000 vaccinations.

A murine strain of Mexican origin obtained from Mooser gave results similar to those obtained with the historic strains. The starting material in the case of the murine strain was a suspension made from tunica vaginalis scrapings.

As many as 49 successive yolk-sac passages were made from one of the strains of *R. prowazeki*.

John W D Megaw

KLIGLER I J & OLEINIK E Presence of a Labile Toxin in Yolk-Sac Cultures of Rickettsia [Correspondence.] *Nature* 1944 Oct 7 462.

The authors have investigated the properties of a highly-labile toxin whose occurrence in suspensions of rickettsiae infected organs of animals was discovered

The drugs did not completely destroy the rickettsiae as was shown by the fact that suspensions of the lungs of the treated mice were still infective though very much less so than suspensions made from untreated mice.

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The author discusses 26 outbreaks of typhus fever in which altogether 113 persons were attacked, in the Provinces of Zaragoza and Navarra during the years 1941-1943.

The paper deals chiefly with the special problems that arose in connexion with the campaign against the disease in the above two areas. Different methods of control were called for in rural as contrasted with urban regions and also in persons of high social status as compared with the poorer classes of the community. So many factors had to be taken into account that the selection of the most suitable plan of action made great demands on the versatility and tact of the officers of health. The relations between these officers and the private practitioners do not always seem to have been happy especially in the large towns.

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by GIROUD [this Bulletin 1938 v 35 791] GILDEMEISTER and HAAGEN [*Dent med Week* 1940 v 66 979] found that the same toxin occurred in yolk sac cultures.

Suspensions of rickettsiae were prepared from yolk-sac cultures and centrifuged. The supernatant fluid when injected intradermally into rabbits produced necrotic skin lesions similar to those described by Giroud. This effect was observed even when the fluid was diluted 20-40 times and even in cases in which the supernatant fluid obtained from cultures of the murine strain failed to infect mice or rats.

Suspensions made from the sedimented rickettsiae were at least twice as toxic as those made from the supernatant fluid, and their toxicity was not reduced by alternate freezing and thawing repeated 7-8 times, although this process destroyed the infectivity of the rickettsiae.

The toxin was found both in human (louse-borne) and murine (flea-borne) strains, and its effects when injected intraperitoneally into rabbits, mice and rats were similar irrespective of which strain was used in its preparation.

The toxin, both in supernatant fluid and rickettsial suspensions was completely inactivated by heating for half an hour at 56-60°C. but was not affected at 40°C. Culture suspensions mixed with an equal volume of distilled water lost their toxicity after being kept for three days at 37°C. Supernatant fluid and suspensions lost their toxicity after shaking with ether for half an hour followed by complete removal of the ether.

Culture suspensions were rapidly frozen and thawed 7-8 times and then centrifuged. The toxicity of the supernatant fluid was greater than that of fluid obtained in the same way from untreated suspensions although freezing and thawing of supernatant fluid free from rickettsiae caused some loss of toxicity. It appeared, therefore that the process of freezing and thawing liberated toxins from the rickettsiae in amounts which more than compensated for the reduction caused by its action on the free toxins.

The work has not yet dealt with the question of the antigenetic properties of the toxins, but in the respects in which they have been studied those prepared from two strains of rickettsiae were indistinguishable from each other.

John W D McGon

SIXON B. A Report on Thirty Cases of Typhus Fever (Louse Borne). *Indian Med Gaz* 1944 Apr v 79 No 4 148-50 6 charts.

The author saw these cases while he was pathologist in the Persia Iraq Field Force in 1943 when the disease was raging in epidemic form in certain localities among the civilian population. The attacks occurred sporadically among persons who had been in contact with the local population in the course of their duties.

In 3 mild cases the fever lasted 6-9 days. One of these patients had been vaccinated against typhus 3 months earlier with Cox's vaccine.

In 17 severe non-fatal cases drowsiness was apparent by the 3rd or 4th day, mental confusion and bouts of delirium were usually observed by the 5th or 6th day. Two of these patients escaped from hospital and were found wandering some distance away. The average duration of the fever in this group was 17 days.

Between the above groups came eight cases of moderate severity with an average duration of 14 days. One of the patients had been vaccinated six weeks before the onset.

There were three deaths, but one of these, which occurred on the 39th day was attributed to tuberculous pleurisy and a severe staphylococcus infection. The two deaths regarded as due to typhus infection occurred on the 13th and 20th days. The patients were the only ones belonging to the 40-50 age group.

The agglutination titre with *Proteus O\19* rose to 1-500 or over in all the cases in which repeated tests could be carried out but in only 12 cases a diagnostic rise in titre (1-250 or over) was observed before the 9th day in the remaining 18 cases this titre was reached in 10-10 days.

The OAA titre was as high as the O\19 titre in 9 of the 23 cases in which it was tested. The O\2 titre was relatively low but in three cases in which the maximum O\19 titre was 1-250 the O\2 titre rose to 1-500.

Leucocyto counts were made in 20 cases the highest total observed was 10 000 the lowest 3 752 and the average 5 776.

The blood sedimentation rate was tested in five cases in the 1st week it averaged 15 mm (Westergren) in the 3rd week 38 mm and in the 9th week 12 mm.

John W D Megaw

ASCHENBRENNER R Ueber urämische Zustände beim Fleckfieber [The Uraemic Condition in Typhus Fever] *Alin Woch* 1944 Jan 22 v 23 No 1/4 8-12 1 chart [Numerous refs.]

The author discusses at considerable length the causes of the great increase in the blood urea observed in some cases of typhus fever.

In one patient whose attack was mild and was followed by rapid convalescence the blood urea rose to 295 mgm per cent on the 9th day and fell rapidly to normal within a period of eight days. There was a negligible degree of hypochloræmia and only slight albuminuria. The urinary sediment showed numerous leucocytes erythrocytes and cylindrical casts.

In another patient who had severe cerebral symptoms bronchopneumonia and other complications followed by death on the 17th day the blood urea which had been 35 mgm on the 10th day rose to 320 mgm on the 17th day. The autopsy report stated that the kidney changes did not amount to glomerulonephritis. In this case also albuminuria was slight on the 13th day a few cylindrical casts erythrocytes and leucocytes were found in the urine.

In still another patient who had severe cerebral symptoms the blood urea was 41 mgm on the 10th day and rose to 292 mgm on the 14th day when it was found that his bladder was enormously distended and nearly 4 litres of urine were withdrawn by catheterization. Within 24 hours the blood urea had fallen to 59 mgm and by the 17th day it was only 34 mgm.

There were no clinical indications of the increase in the blood urea which is called by the author a uraemic condition and is regarded as differing sharply from a hypochloræmic uraemia.

The only explanation offered by the author is an increased production and diminished excretion of urea the diminished excretion being due to damage to the kidney of an inflammatory or functional nature.

John W D Megaw

RAETIG H Gibt es Fleckfieberrückfälle? [Do Relapses occur in Typhus Fever?] *Deut med Woch* 1944 May 12 v 70 No 19/20 274-5 2 figs.

Among 500 cases of typhus fever observed by the author there were two in which the occurrence of a relapse was regarded as having been proved. Mention is made of two other cases in which a relapse was suspected in both of these the initial fever lasted 12 days and terminated by crisis. After an afebrile period of three days there was a second rise of temperature cerebral symptoms appeared within two days and both of the patients died of circulatory failure.

It is mentioned that both of them had been given intravenous injections of convalescent serum early in the initial attack.

Fuller details illustrated by temperature charts are given of the two cases in which relapse was regarded as having been proved. In one of these the initial period of fever lasted about 11 days and ended by lysis. The temperature remained normal for two days, then there was low continued fever with a pulse rate of about 82-85 for five days. The temperature rose suddenly on the 18th day and remained high till the 29th day when death occurred. The diagnosis of typhus fever was confirmed at the autopsy. A scanty "typical typhus rash" is described as having occurred on the 6th day and on the 24th day a characteristic rash appeared on the trunk and limbs. This patient received 60 cc. convalescent serum on the 5th day.

In the second, undoubted, case the initial fever lasted nine days and ended by crisis. A low-grade typical rash was seen on the 5th day. An aleuric period lasting 10 days was followed by a rapid rise of temperature to 39.7°C. High continued fever lasted for six days and was followed by a period of gradual lysis—the temperature became normal on the 37th day.

The Weil-Felix titre was 1-400 on the 13th day and 1-800 on the 34th day. These are the only Weil-Felix tests mentioned in the paper. This patient also was treated by convalescent serum—70 cc. on the 6th day.

[From the charts illustrating the reports of these two proved cases of relapse it is seen that the pulse rates during the initial attacks were decidedly low—in the first case the rate exceeded 80 on only two occasions, in the second it ranged from 60 to 68 except for one occasion although the temperature twice rose above 40°C. During the second febrile periods the pulse rates, though relatively low were such as might be expected in attacks of typhus fever. Sceptics will hardly accept the evidence contained in the paper as proof of the occurrence of relapses in typhus fever. The question may even be raised of the possibility of the relapses being primary attacks caused by infection introduced with the convalescent serum.]

John W. D. Mcgregor

BRANDENBURGER P. Zur Behandlung des Fleckfiebers. [The Treatment of Typhus Fever] *Deut. med. Woch.* 1944 June 9 v 70 No 23/24 329-31

The author's views are based on an extensive experience in the treatment of typhus fever on the Eastern Front—often in very unfavourable conditions. The fatality rate was only about 8.5 per cent.

He adopts a refreshingly critical attitude towards the numerous claims that have been made by other German physicians for the efficacy of various drugs. He rightly points out that such claims must be received with caution, based as they have been on experience of a limited number of cases and without adequate controls.

He insists that the predominant lesions are those of the brain and that the state of coma resulting from these cannot be influenced by any drugs. Some of the views expressed in this important paper are as follows—Overdosage with such drugs as cardiazol, coramin and strychnine is quite useless. circulatory failure does not play a leading part in causing the state of collapse so much emphasized by STURM [this *Bulletin* 1943 v 40 381] and others. The fall in the blood pressure is not checked by camphor or adrenaline derivatives. dosage with these drugs has often been suspended without the slightest adverse effect.

The myocarditis of typhus fever is influenced by digitalis and strophanthin to exactly the same degree as that due to other causes.

Calcium sulphonamides and atabrin were not found to have any appreciable value. Hypertonic solutions of glucose given intravenously had no obvious effect on "cerebral pains." Injections for the relief of pain were avoided. Lumbar puncture often had an adverse effect on the encephalitic symptoms.

Convalescent blood for practical reasons, could only be given by intramuscular injection, by this route it had no obvious effect. Injections of cortison [desoxycorticosterone acetate] were seldom found to be effective. Vitamin therapy was widely used but no striking benefit was observed.

Altogether little help was obtained from drugs and reliance was placed on well-organized and watchful care of the patients.

Plenty of liquid was given the patients readily took two to three litres daily in the early stages and after lethargy had set in great care was needed to prevent dehydration when necessary intravenous salines with glucose were given at frequent intervals.

Fresh air uniform ward temperature and the avoidance of draughts are important. Even in summer the wards should be heated on cold days.

Luminal [Phenobarbitone] sometimes aggravated the condition of delirium good results were obtained from small doses of scopolamin-eucodal ephetonin given subcutaneously in the evening [Eucodal (Merck) is dihydro-hydroxy codemone hydrochloride].

When possible the patients were allowed to take their meals sitting up in bed and to pass urine and stools into a low commode by the bedside.

The diet was generous and varied the tastes of the patients were humoured and they were encouraged to take and thoroughly masticate such articles of diet as rusks bread and butter fruits etc. On this régime the condition of the mouth remained healthy and parotitis was almost unknown. Invalid diets were avoided even in the frequent cases in which diarrhoea was a prominent feature.

John W D Megaw

SCHULTEN H. Das Fleckfieber bei Geimpften. [Typhus Fever in Inoculated Persons.] *Alin Woch* 1944 Jan. 22 & 23 No 1/4 12-13 1 chart

The author admits the difficulty especially in field conditions of making a satisfactory estimate of the severity of attacks of typhus fever in inoculated as contrasted with unprotected persons.

His observations were made on 195 patients who had been vaccinated within the preceding six months—the method is not stated—and 100 control patients. The distribution figures are percentages.

	Very mild	Mild	Moderate	Severe	Fatal	Average duration
Inoculated	4	52	37	5	2	12-06 days
Controls	1	29	50	13	7	15 23 days

The average age of the inoculated was 32-83 years of the controls 28-08 years

John W D Megaw

RUIZ CASTAÑEDA M. Preparación de vacuna antityfo bivalente. [Preparation of Bivalent Antityphus Vaccine.] *Rev Inst Salubridad y Enfermedades Trop Mexico* 1944 Mar v 5 No 1 1-9 English summary (3 lines)

In this paper full details are given of the technique now employed by the author in the preparation of a bivalent antityphus vaccine which he regards as preferable to the monovalent vaccine because he believes that epidemics of louse-borne typhus may originate from murine as well as from classical strains of rickettsiae.

The lungs of mice and rats inoculated by the intratracheal route are used and there are certain differences in the methods employed in preparing the two types

of vaccine which are afterwards mixed together in a concentrated suspension to which formalin is added as a preservative. The mixture is diluted with saline at the time of use.

Except for workers who contemplate undertaking the difficult work of preparing animal-lung vaccines the author's previous description of the bivalent vaccine will suffice [see this *Bulletin* 1943 v 40 128] *John W D Meyer*

PATTERSON H. S. Scrub Typhus: an Unusual Case simulating Mumps. *Med J Australia* 1944 Aug. 5 v 2 No 6 133.

In this case the onset was with painful swelling in the region of the right parotid gland and redness in the upper eyelid of the right eye. On the 2nd day a small scabbed lesion was noticed in the middle of the margin of the reddened eyelid.

From the 2nd to the 4th day the temperature was remittent and ranged between 99.4 and 101.4°F. The provisional diagnosis was mumps.

On the 4th day a pink macular rash appeared on the trunk, and the temperature rose to 103.4. There was bilateral axillary adenitis, severe frontal headache and backache. Attention was drawn at this time to the resemblance of the lesion of the eyelid to the eschar of typhus fever (presumably the initial necrotic sore often seen in mite-borne typhus is referred to).

The provisional diagnosis was then changed to one of scrub typhus and this was confirmed by the Weil-Felix agglutination test which was performed a week later, a serum-agglutination of 1-1,280 being obtained. [The strain of *Proteus* organism used in the test is not mentioned.]

By the 5th day the rash became confluent and extended to the limbs. A bilateral inguinal adenitis was observed on the same day. The further course of the illness does not call for special comment: it was such as would be expected in a case of mite-borne typhus. *John W D Meyer*

WOMERSLEY H & HEARLIF W G. The Trombiculinae (Acarina) or Hishmalies of the Austro-Malayan and Oriental Regions. *Trans Roy Soc S Australia* 1943 v 67 Pt. 1 86-142, 12 pls. & 18 figs. [59 refs.] [Summary taken from *Rev Applied Entom* Ser B 1944 Sept. v 32 Pt. 9 161-2.]

This paper includes a brief discussion of the economic importance of the mites of the subfamily Trombiculinae, a key to the 19 genera recognised by the authors (of which two are new and a third receives a new name) and a revision of the species of the Austro-Malayan and Oriental Regions. The many new species described include *Trombicula fletcheri* which occurs in Malaya and is thought to be the species recorded there as *T. akamushi* Brumpt, and *T. hatori* which is the Formosan mite briefly described by Hatori as *T. pseudoakamushi* (non Tanaka) and described and figured by Kawamura and Yamaguchi as *T. pseudoakamushi* (non Tanaka) Hatori. In the section on economic importance it is pointed out that though Trombiculine mites of several genera attack man and cause severe irritation, all those that are vectors of disease belong to the genus *Trombicula* sens. str. *T. akamushi* is the recognised vector of tsutsugamushi disease in Japan and Formosa, and *T. deliusi* Walch probably transmits the same or an allied disease in Sumatra, Malaya, Queensland and India. The name *T. minor* var. *deliusi* Walch* is used for the mite that Gunther considered to be the vector of endemic typhus in New Guinea. Gunther described it as *T. kirsi* var. *bulolensis* [but later concluded that it was identical with *T. minor* Berl.]

*The name *deliusi* as applied to this form is preoccupied by Walch's species *T. deliusi*. The next available name for the variety is presumably *bulolensis* Gunther.—Ed.

As regards the nomenclature of the Japanese species the author considers that *T pseudoakamushi* Tanaka should be dropped from the literature as it is a complex of at least two species for which valid names (*T pallida* Nagayo et al.) and *T palpalis* Nagayo et al.) are available but he has been unable to ascertain the status of *T tanakai* Kishida which may be an earlier name for *T akamushi*.

PRADHAN K G Typhus in Akola (Berar) *Indian Med Gaz* 1944 Apr v 79 No 4 145

Since 1937 the author has seen 50 cases of fever diagnosed as typhus at Akola a town in Berar in central India. About 8-10 cases were seen yearly all in the months of August September and October. The mortality rate was about 10 per cent.

The clinical description given by the author is in keeping with his diagnosis of a fever of the typhus group. The fever lasted about 14 days it was of the continued or remittent type except in one case in which it was almost intermittent it ended by lysis. The rash appeared about the 6th day it extended over the whole body except the palms and soles and was macular and haemorrhagic in the severe cases in mild attacks it was papular. Toxaemia bronchitis and albuminuria were features of all except the mildest cases. The Weil Felix reaction was inconclusive in the one case in which it was tested. Most of the patients were poor persons and were louse infested but some were free from lice some were cultivators and tick typhus was regarded as a possible diagnosis. In one child a jungle tick was suggested as a probable insect vector.

John H D Megaw.

BARDHAN P N Typhus in the United Provinces of India Being a Contribution to the Study of Typhus Fever *Indian Med Gaz* 1944 Apr v 79 No 4 150-54

The author saw 41 serologically proved cases of typhus fever in the United Provinces of India where the disease is said to occur in a mildly endemic form throughout the year. All the patients were in the Army there were no complications and no deaths.

In 1937-1938 the author saw 11 cases in Lansdowne Cantonment, which is situated at an elevation of 6000 feet in the same range of hills as Kumaon, from where Megaw (1917) Blewitt (1938) and other workers have described cases of tick and louse-borne typhus.

Ticks lice and bed-bugs are said to abound in the place but not in the military living quarters. Platoons of troops often went to the neighbouring hills where they camped up to 8 days at a time.

The clinical description points to the diagnosis of a relatively mild fever of the typhus group but surprisingly no rash could be detected in any of the patients. The leucocyte count was normal or slightly raised it was never below normal.

The remaining 30 cases were seen at Jhansi (19 cases) Nowgong Muttra and Agra all in the plains of the United Provinces in 1939-1942.

These were similar in their clinical features including the absence of rash. Thirteen of the cases occurred in the cold weather months of December January and February the rest were rather uniformly distributed over the other months except that only two occurred in July and August.

All the patients would be exposed to bites by fleas sandflies and ticks and mites during outdoor training lice were well under control and generally absent.

The agglutination responses in the two groups of cases were remarkably similar: tables show the titres observed in each case from the 4th day onwards. From these it appears that the *Proteus OX19* and *Pr OX2* titres never exceeded 1-80 and showed only a slight tendency to rise during the febrile stage. The *OXK* titres in the two groups can be gathered from the following analysis of the tables —

Proteus OXA Titres

Day of Disease	4	9	13-14	15	20	30
1st Group						
1-50 to 1-125	10	8	8	—	—	—
1-250 to 1-500	0	3	8	—	—	—
2nd Group						
1-25 to 1-125	28	17	—	8	10	18
1-250 to 1-500	2	13*	—	22*	20	5

Including one titre of 1-1 000.

The *OXK* titre was 1-125 or 1-250 as early as the 4th day in 15 of the 41 patients: these and the other unusual agglutination responses suggest that it would be interesting to check the *Proteus* strains used in carrying out the tests.

John W D Meigan

HEILIG R. & NAIDU V. R. Complement Fixation Tests performed by N. H. TOPPING, U.S. Public Health Service, and other Observations in Mysore Typhus. *Indian Med Gaz* 1944 Apr v 79 No 4 154-7 [13 refs.]
INDIAN MED GAZ 1944 Apr v 79 No 4 173 Typhus Fevers in India.

Additional information is given about the fever of the typhus group already described on several occasions by the authors as occurring in Mysore City and State. Among 32 patients only two were members of the same family. A leucocyte count of 12,000 to 20,000 was a constant feature.

The Weil-Felix responses of the additional 18 patients dealt with in the present paper are shown in a table from which it appears that *Proteus OX19* was agglutinated in titres of 1-80 or over in 6 cases and that in one exceptional case the titre rose to 1-1,280 on the 11th day and to 1-20,000 on the 13th day. In this case death occurred on the 16th day. Apart from this case the titre exceeded 1-80 in only two patients: in one of these it was 1-320 from about the 5th to the 11th day; it fell to 1-160 on the 13th day and remained constantly at that height till the 18th day.

The *OX2* titre was 1-80 or over in 16 patients: the highest titre recorded was 1-320.

The *OXK* titre was 1-80 or over in six patients: the highest recorded was 1-320 on the 9th day; in this case it fell to 1-40 on the 13th day.

The agglutination titres are said to "vary quickly and sometimes the agglutinins are present only for a short time."

The Neill-Mooser reaction (presumably in guinea-pigs) was positive in four cases and negative in 12. From a guinea-pig inoculated with the blood of one of the patients S. R. SAVOON has isolated and maintained a strain of rickettsia through repeated guinea-pig passages for 8 months: this was an orchitic strain. Another orchitic strain died out after several passages.

The interesting results of complement-fixation tests carried out by N. H. TOPPING are again mentioned: these in Topping's own words "would seem

to indicate that the disease which you consider to be endemic typhus in Mysore is caused by a virus which produces antibody that fixes complement to a higher titre with a rickettsial antigen from Rocky Mountain spotted fever than it does with a rickettsial antigen prepared from either endemic or epidemic typhus

The disease is regarded by the authors as being probably tick borne and as being serologically and clinically identical with Boyd's No. 2 typhus [this *Bulletin* 1936 v 33 417] which certainly is not a louse-mite or rat flea typhus

None of the patients had obvious contact with jungle ticks so that dog ticks were regarded as the probable local vectors.

John W D Megaw

BEIGLBOCK W & LÖSCHER H Zur Behandlung des Wolhynischen Fiebers.
[The Treatment of Trench Fever] *Deut med Woch* 1944 Mar 3 v 70
No 9/10 120-23 2 charts.

The authors begin by stating that none of the methods of treating trench fever hitherto tried has been found successful. It occurred to them that the recurring attacks of fever which are characteristic of the disease might represent a defensive reaction on the part of the body as well as a symptom and so they decided to try pyretotherapy. They found that an intravenous injection of 0.5-1.0 cc. of pyrifin [a colon bacillus vaccine] caused a sharp rise of temperature to a higher level than that occurring in the natural paroxysm. They decided that the best time to start treatment was after the end of a spell of fever but in some chronic cases with slight rises of temperature they gave the injections during the febrile periods.

After experience gained in the treatment of 25 patients they formed the opinion that one or two—in rare cases three—injections at intervals of 3-4 days were enough to cut short the course of the disease. In some cases pyrifin of number 1 strength did not cause a sufficiently sharp reaction and in these cases the next injection consisted of number 2 strength of the preparation. They admit that it is very difficult to estimate the effect of any treatment in a disease so variable as trench fever and also that the only available control was their experience of previous cases treated either without drugs or by sulphapyridine or atabrin. Still they claim to have established the value of the treatment beyond any reasonable doubt.

Clinical details illustrated by temperature charts are given of two cases. A further claim is made that there is great relief of pain and a rapid return to normal of the blood-sedimentation rate.

John W D Megaw

EBERLIN E. Ueber die Behandlung des Wolhynischen Fiebers (Fünftagefiebers) mit Antimonpräparaten [The Treatment of Trench Fever with Antimony Preparations.] *Deut med Woch* 1944 May 26 v 70 No 21/22 306
2 figs.

In a series of cases of trench fever the author found that the fever and the shin pains were quickly cured by solustibosan (Bayer) [hexonate or gliconate of antimony in pentavalent form]. A daily injection [dose not stated] for three successive days was given. It can be given intramuscularly as well as intravenously and produces no unpleasant side-effects

J F Corson

Tropical Diseases Bulletin.

YELLOW FEVER.

CHANDLER A. C. Phenothiazine as a Mosquito Larvicide with special reference to Container-breeding Mosquitoes. *Proc. & Papers 13th Ann. Conference Mosquito Control Ass.* 1944 Feb 23 & 29 Berkeley Ca 86-60

The author claims that phenothiazine is the ideal larvicide for controlling the breeding of *Aedes aegypti* in fire buckets, drinking troughs, vases in cemeteries and such like. The powdered chemical dusted on the surface at the rate of 2 gm. per 25 gallons of water will prevent breeding for three months to one year after a single application. For use to the public for use in flower vases, etc. it may be incorporated with glue and applied to paper (4 gm. phenothiazine to 100 sq. in. of paper) and cut into pieces $\frac{1}{2} \times 1$ in. or for use by sanitary inspectors, it may be suspended in dilute alcohol and applied from a dropper bottle in amounts to give a concentration of something like 1 in 80 000 parts of water. Phenothiazine is highly toxic to fish.

DENGUE.

DAGGETT R. H. *Aedes scutellaris hybridus* Edwards. A Probable Vector of Dengue in the New Hebrides. *War Medicine* Chicago. 1944 May v 3 No 5 292-3.

During an epidemic of dengue among troops stationed on the island of Espiritu Santo in the New Hebrides, *Aedes scutellaris hybridus* was found breeding in large numbers in the usual artificial containers as well as in coconut shells, cacao pods, etc., at a time when *Aedes aegypti* was very scarce. This is regarded as good epidemiological evidence that *Aedes scutellaris hybridus* is a carrier of dengue. This species is closely related to *A. albopictus* which is a proved carrier in the Philippines. It breeds in small collections of water and around houses like *A. aegypti* but in addition it breeds in the forest rain-filled holes, in raised coral reefs and in open wells. B Wigglesworth

PLAGUE.

PUBLIC HEALTH REP. Wash. 1944 July 14 v 88 No. 28 911-15 Plague Infection reported in the United States during 1943.

In the United States only two cases of plague occurred during 1943 one of which was fatal. This fatal case, in a child of two years of age, is especially interesting because death occurred two months after onset, and the diagnosis at autopsy was "bubonic plague and chronic plague encephalitis." Field surveys continued as in previous years and several new localities were reported infected. The rodents found to be plague-infected were rats, ground squirrels, chipmunks, wood rats, meadow mice, harvest mice, white-footed mice, grasshopper mice and prairie dogs. Their ectoparasites were fleas, lice and ticks. Surveys are necessarily only of sampling type, but the "wide biological and geographic distribution of plague infection in western United States will serve to give a warning if the areas of syriatic infection approach localities sufficient biological densities of susceptible rodent species and human populations to constitute a dangerous situation." W F Harvey

PUBLIC HEALTH REP Wash 1944 July 21 v 59 No 29 962. Human Case of Pneumonic Plague (Laboratory Infection) in San Francisco, Calif.

A case of primary pneumonic plague in which the infection was acquired in the laboratory has been reported in San Francisco Calif. The case occurred in a Public Health Service Officer who was engaged at the time in plague work at the plague laboratory in San Francisco. The patient became ill on May 30 and was admitted to the United States Marine Hospital on June 1. He is reported to have recovered. Precautionary measures were promptly adopted and no secondary cases have occurred.

BLANC G & BALTAZARD M. Sur le mécanisme de la transmission de la peste par *Xenopsylla cheopis* [The Mechanism of Transmission of Plague by *Xenopsylla cheopis*] C R Soc Biol 1942 Oct v 136 No 19-20 646-7

It is generally accepted that obstruction of the proventriculus of *Xenopsylla cheopis* by plague bacilli with subsequent vomiting while biting is an important means of transmission of plague. The authors have made experiments which lead them to discredit the importance of this blocking of the fleas.

A guinea pig with a heavy blood infection with plague bacilli was placed in a box along with fleas *Xenopsylla cheopis* which had been kept for 15 days after being bred out and had not yet fed. This is known to produce infection in 100 per cent of the fleas but to make sure other similarly infected guinea pigs were put into the box for a few days. Then healthy guinea pigs were placed successively in the box and left there until they died. 15 guinea pigs thus died of plague in the box which was cleaned frequently to avoid the inclusion of new fleas. The experiment lasted for three months and during the last 15 days only a few fleas remained alive but three months is the duration of life of the fleas in all breeding and experimental boxes so there was no abnormal mortality in the box though it is generally believed that blocked fleas die rapidly of starvation. Since all the fleas were infected from the start of the experiment transmission was obtained throughout three months if this was only effected by blocked fleas either the blocking persisted for three months or still more unlikely the fleas became blocked successively.

The authors think that the chief factor is the multiplication of the bacilli in fresh blood taken up in frequent feeds. Experiments have shown that infected *Xenopsylla cheopis* after a fast of 15 days are unable to infect by their first bite but become infective less than 12 hours afterwards. It seems that the intake of fresh blood permits the multiplication of the bacilli in the digestive tube and favours their passage into the proventriculus and proboscis. This view is supported by the positive results of experiments with lice fleas bugs and ticks in which blocking does not occur.

The inability of *Xenopsylla cheopis* to infect at the first feed after a fast is of epidemiological importance since the fleas only attack man when urged by hunger and leave him at the first opportunity afterwards. J F Corson

SAVINO E & KUSNETZ GOEBAR J. La peste rural en el departamento de Rio Seco (Córdoba). Su estudio epidemiológico con especial referencia al *Graomys griseoflavus centralis* como depósito de virus pestoso así como también el hallazgo de peste espontánea en algunos roedores agrestes y en gatos domésticos. [Rural Plague in Rio Seco, *Graomys griseoflavus* as Reservoir and the Discovery of Plague in Field Rodents and Cats.] Bol Sanitario Buenos Aires. 1943 July-Sept. v 7 Nos. 7 8 & 9 193-200 [14 refs.]

The results of the authors survey were (1) *Graomys griseoflavus centralis* Twenty-eight were examined and from 24 of these 60 fleas mostly

YELLOW FEVER.

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The results of the authors survey were (1) *Graomys griseoflavus* Twenty-eight were examined and from 24 of them

Rhopalopsyllus were collected. Two *Graomys* one dead and one moribund yielded positive plague cultures. These rodents it was confirmed, have contacts with human habitations. (2) Other rodents identified were *Galus muridoides leucoblephara*, *Hesperomys murillus cordosensis* and *Mus musculus*. (3) Cats. Five cats had died spontaneously and three of these were proven plague-infected the other two were negative.

POZZO A. A. Peste selvatica—peste silvestre. [Sylvatic Plague.] *Bol. Sanitario* Buenos Aires. 1943 July-Sept., v 7 Nos. 7 8 & 9 255-64

CHOLERA

- I. BERNARD P N & GALLUT J Sur un mode de préparation de la toxine cholérique. [A Method of Preparation of Cholera Toxin.] *C R Soc. Biol.* 1943 Jan. v 137 No 1-2 10
- II. ——— & ——— Conditions favorables à la production de la toxine cholérique. [Conditions Favourable for the Production of Cholera Toxin.] *C R Soc. Biol.* 1943 Jan v 137 No 1-2, 11-12.

I. The culture medium is the peptonized broth containing glucose and sodium acetate used by RAMON [Bulletin of Hygiene 1933 v 8 295] for obtaining diphtheria toxin. Cholera vibrios grown on agar for 18 hours at 37°C. are added in the proportion corresponding to 8-10 mgm. of dried organisms to 1 cc. of broth portions removed for testing after the addition of toluene are centrifuged to get rid of the vibrios. The toxin appears in the supernatant liquid after three hours reaches a maximum after four hours and rapidly diminishes after five hours. At four hours the fatal dose for a guinea pig of 250 gm. is 0.25 cc. and for a mouse of 15 gm. it is 0.05 cc.

A more powerful toxin can be obtained by repeatedly adding more vibrios to the same broth (250-500 cc.) centrifuging it four hours after each addition, and replacing the glucose to its original strength of 5 gm. per litre and readjusting it to pH 8. After the tenth addition of 5 gm. per litre and readjusting fatal dose for a guinea pig of 0.05 cc. it may even disappear entirely decreases after the fifth addition or it may even disappear entirely.

ii. In the preparation of cholera toxin described above 89.5-100 per cent of the vibrios are dead after four hours incubation and the pH of the medium has changed from 8 to 5.8 in the same broth without glucose few vibrios die. The change in the pH is produced by fermentation of the sugar by the vibrios with the equivalent of 2 mgm. of dry vibrios per cc. of broth the pH reaches 5.8 in five hours and 3.8 gm. of the original 5 gm. per litre of glucose has been used up. Estimations made with different quantities show that the most favourable proportions are 5 gm. of glucose per litre and the equivalent of 8-10 mgm. of dry vibrios per cc. In the authors' experiments the massive death of the vibrios appears to be the dominant factor in the rapid diffusion of the cholera toxin.

J F Corson.

BACILLARY DYSENTERY

STEWART W On the Viability and Transmission of Dysentery Bacilli by Flies in North Africa. *J Roy Army Med. Corps* 1944 July v 83 No. 42-6.

Human carriers of dysentery bacilli—Flexner Sonne and Schmitz—common among the native population, in Algeria. Of 149 Arabs examined

employment in kitchens 23 gave positive stool cultures they were apparently well and their stools were normal in appearance Hygienic standards are low and the natives urinate and defecate in open spaces and open latrines Myriads of flies breed and feed on such excreta during the hot season Experiments were therefore planned to find what part the fly may play in the spread of dysentery Positive specimens of faeces spread on uncovered Petri dishes were placed along with trapped flies in a composition box covered with mosquito-proof netting the contents were exposed to the air but not to direct sunlight The faecal specimens dried up in 1 to 2 days Drinking water was supplied—otherwise the flies died in 2 to 3 days but as Flexner bacilli were found to survive in plain water for 38 days the water supply was changed regularly so as to prevent its becoming a source of infection Plates of MacConkey's medium were placed in the box removed at regular intervals after being naturally inoculated by the flies and after incubation were examined for colonies of the dysentery organisms Under these conditions flies could apparently carry dysentery bacilli (Flexner and Schmitz) for periods up to 11-12 days As dysentery organisms could not usually be recovered after 1-2 days from faeces allowed to dry naturally it is apparently presumed that flies would not be contaminated from the specimen after this time However in the author's own experience dysentery bacilli may remain viable in faeces for 5 8 10 and 12 days (four different specimens) Although flies were shown to be carriers the incidence of dysentery in this particular area dropped sharply in August and September when flies were still prevalent.

Robert Cruickshank

POTH E J & Ross C A The Clinical Use of Phthalylsulphathiazole J Lab & Clin Med 1944 Aug 29 No 8 785-808 13 charts [21 refs]

Phthalylsulphathiazole is a compound the properties of which have been described in previous abstracts (this Bulletin 1944 v 41 757) It closely resembles succinylsulphathiazole but is two to four times more active When given to dogs by mouth it reduces the coliform bacilli in the faeces to very small numbers and suppresses the anaerobic vegetative organisms (but not the spores) it is ineffective against *Strep faecalis* It renders the faeces less liquid than does succinylsulphathiazole It may be given to man in doses of 0.0625 to 0.25 gm per kgm per day divided into three to six doses or as a single dose The lower the total daily dose and the less it is subdivided the slower the action in reducing the faecal content of coliform bacilli When 0.25 gm per kgm is given daily divided into six doses these bacteria were greatly reduced in number (to 10 bacilli per gm. wet stool) even in the presence of watery diarrhoea produced by magnesium sulphate in this respect phthalylsulphathiazole is more effective than succinylsulphathiazole Apparently relatively more of the phthalyl than of the succinyl compound is converted into free sulphathiazole in the bowel. The amount of phthalylsulphathiazole which is absorbed into the body (as judged by the amount excreted in the urine) is not increased by increasing the dose consequently increasing the dose does not increase the toxicity There is some evidence that the bacteriostatic action of the bowel is not due entirely to the sulphathiazole liberated but that part of it may be due to the unchanged drug

Other sulphonamides—sulphanilamide sulphapyridine and sulphathiazole—have little or no action in reducing the numbers of coliform bacilli in the human faeces when given by mouth but admittedly they are often effective in the treatment of bacillary dysentery

Phthalylsulphathiazole has proved to be highly specific in the treatment of (Flexner) bacillary dysentery [POTH this Bulletin 1944 v 41 570] It is also in non-specific diarrhoeas The best

per kgm. every four hours for 12 doses, and then 0.02 gm. per kgm. at four hour intervals until diarrhoea ceases, or for a total of seven days. Positive stools are found only rarely on follow-up cultures if they are found, the patients should be given 0.02 gm. per kgm. every four hours for 10 more days after which further cultures should be made.

Six cases of chronic ulcerative colitis have been treated, with a satisfactory clinical response in every instance. During the initial period of four weeks, 0.02 gm. per kgm. was given every four hours. One patient has been treated continuously for 10 months, without any toxic reactions.

Phthalylsulphathiazole is also recommended for preparatory treatment of patients before operation on the large intestine being better in this respect than succinylsulphathiazole if diarrhoea is present. The dose is 0.02 gm. per kgm. four hourly. Toxic reactions have been rare, a single case of drug fever being the main instance. Crystalluria does not occur. *F. Hawking*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

BELTRÁN, E. & RAÚL LARENAS M. Investigación de protozoarios en materias fecales de niños con diarrea. [Protozoa in the Faeces of Children with Diarrhoea.] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico 1944 Mar v 5 No. 1 23-30. English summary.

"Fecal samples of 1,500 children with diarrhetic stools were examined for protozoa. Ages of same were from 0 months to 6 years. In those groups of less age (0 to 6 months, 7 to 12 months and 13 months to less than 2 years) the general parasitisation was low: 4 per cent., 13 per cent. and 33 per cent., respectively; so was also the incidence of *E. histolytica*: 0.3 per cent., 0.5 per cent. and 2 per cent. In those groups of higher age (2 to less than 3 years and 3 to 6 years) the parasitisation was notably higher (62 per cent. and 59 per cent.) as well as the incidence of *E. histolytica*: 16 per cent. and 17 per cent. respectively. The results obtained seem to show the slight importance of protozoa

etiology of infant's diarrhoeas at least under 2 years ago. [The work was done in Mexico City.]

REES, C. W., BOMICKVICH, J., REARDON, LUCY V. & DAFT, F. S. The Influence of Cholesterol and certain Vitamins on the Growth of *Endamoeba histolytica* with a Single Species of Bacteria. *Amer. J. Trop. Med.* 1944 May v 24 No. 3 189-93. (10 refs.)

Working with cultures of *E. histolytica* accompanied by a single bacterial species the authors have found that if the whole egg in the L.E.S. medium [this *Bulletin* 1925 v 22 727] which was the one employed, is replaced by egg white or egg yolk, only poor growth is obtained. To media prepared with egg white or yolk various materials were added with a view to discovering some of the essential requirements of the amoebae. The addition, to the egg white medium, of cholesterol and vitamins of the B complex, stimulated growth of amoebae to well over 1,000,000 per flask. This compared very favourably with the growth in the whole egg L.E.S. medium. Cholesterol alone or vitamins alone had no favourable action. These substances did not improve the egg yolk medium, though a combination of ovalbumin, ovomucin and ovomucoid did so. Egg albumin medium was improved by the addition of amino acids of casein hydrolysate or four purin bases. A number of other substances gave indeterminate results. It seems evident that the whole egg

base in the L.E.S. medium supplies substances essential for the growth of amoebae which in flasks of this medium reach 1 530 000 per flask. The general results are set out in a table while many technical details are given in the body of the paper

C M Wenyon

MARTIN R & BEBEY M Sur l'encystement de l'amibe dysentérique [Encystment of the Dysentery Amoeba] *Arch Inst Pasteur d'Algérie* 1944 Mar v 22 No 1 11-12.

In the faeces of a dysenteric patient the authors observed numerous amoebic cysts about 18 microns in diameter. The specimen was very rich in bacteria, many of which occurred within the cysts in an arc extending along one-sixth of the circumference of the cyst. The bacteria were pushing their way through the cyst wall at this arc resting a moment on the wall and then escaping. It is stated that the cysts contained no red blood corpuscles. A similar observation was made on a second case. The authors consider they were observing the process of encystment of *E. histolytica*. As no red blood corpuscles were present these had already been discharged but the bacteria were seen to be escaping through the only remaining permeable part of the cyst wall.

C M Wenyon

GIORDANO A F Urticaria y amebiasis. [Urticaria and Amoebiasis.] *Rev Argentina Dermatosisifilologia* 1944 June v 28 No 2 157-61

The author considers that in cases of allergic skin conditions such as urticaria and angioneurotic oedema intestinal infections are not infrequently the cause. In a series of 27 cases examined by him four were found to harbour *E. histolytica* and one *E. coli* and it is claimed that a cure was obtained by treatment with emetine injections. [Quite apart from the fact that it is generally held that emetine does not eradicate *E. coli* infections the conclusion that the amoebae in the intestine were responsible for the skin condition seems hardly justified by the data presented.]

C M Wenyon

WALTERS W WATKINS C H BUTT H R & MARSHALL J M Amoebic Abscess of the Liver Unsuspected until Perforation. *J Amer Med Ass* 1944 Aug 5 v 125 No 14 963-6 5 figs

Sudden perforation of amoebic abscess occurred in two naval men who had returned to America from the South Pacific area with filariasis. Both patients had been examined and studied in hospital by the Filarial Commission and had shown no signs or symptoms of amoebic abscess. There was no diarrhoea and no amoebae were found in the faeces. In one patient perforation occurred six months after admission to hospital in the other patient after one month. The symptoms after perforation were similar in both—a sudden development of aching pain in the right shoulder in the right costo-vertebral region and in the lower part of the right thorax with chills and fever, pain and muscular spasm were also present in the right upper abdominal quadrant. Radiographs showed progressive elevation of the right side of the diaphragm and loss of the acute cardio-phrenic angle on the left side. There was marked leucocytosis 28 000 cells per cmm. in one case and 19,500 in the other. Both patients had treatment with emetine hydrochloride and an open operation with drainage. Two large communicating abscesses—one in the right lobe of the liver and the other beneath the diaphragm—were present in each patient. The pus was creamy white in colour and contained in one case *Entamoeba histolytica* and

in the other Gram-positive cocci. Both patients made an excellent recovery. The authors refer to papers by BRUNZ [this Bulletin 1943 v. 40 146] and by OCHSNER and DEBAKEY [*ibid.* 915].

J. F. Corson

ROSS J. A. Amoebic Perinephric Abscess. *Brit J Radiology* 1944, Sept. v. 17 No 201 289-90 3 figs.

A case of perinephric abscess occurring in a native serving with the Pioneer Corps in the M.E.F. is recorded. Retrograde pyelography demonstrated the extravasation of the dye from the renal pelvis into the perinephric abscess. An amoebic aetiology was suggested in view of a past history of amoebic dysentery. Anti-amoebic therapy caused a disappearance of the abscess without recourse to surgery thus confirming the amoebic nature of the abscess. [Radiologically an amoebic perinephric abscess is indistinguishable from a perinephric abscess caused by any other organism.]

E. Samuel

DE RIVAS D. Amebiasis of the Uterus. *Amer J Trop Med* 1944 May v. 24 No. 3 183-7 4 figs.

A patient, 70 years of age in a mental hospital, was noted to have a vaginal discharge associated with enlargement of the uterus which suggested malignant disease. After death as a result of senile changes, arterio-sclerosis and hypostatic pneumonia, it was found that the uterus was moderately enlarged and that the swollen cervix was soft eroded and ulcerated. Microscopic examination excluded malignant disease but revealed an ulcerative process and the presence of *E. histolytica* in the granulation tissue. The author believes this to be the first case of amoebiasis of the uterus to be placed on record.

C. M. Weyson

PLACCO F. Amebiasi cutanea (caso clinico) [Cutaneous Amoebiasis]. *Boll. Soc. Ital. di Med. e Igiene Trop.* (Ser. Entrea) 1944 v. 3 No 1 89-94 1 pl. English summary (4 lines).

The author describes a case of cutaneous amoebiasis in the skin of the perianal region.

He points out the rarity of the lesion and difficulty of diagnosis unless a microscopic examination is carried out.

ALEXANDER, J. S. PARK ROSS M. & STEIN M. Shadocol (T.L.P.) in the Treatment of Amebiasis. Preliminary Report. *South African Med J* 1944 Aug 12, v. 18 No 15 253-4.

This study was prompted by a recent paper in the *British Medical Journal* of the successful use of Shadocol in chronic *Salmonella* infections of the bowel.

So far the authors' routine method of treating amoebiasis has been by giving emetine injections, carbamone by mouth and colonic retention enemata of chinacoin (quinovyl, Burroughs Wellcome & Co. Yareen, Bayer). This procedure can be criticized on the following grounds—(a) expense (b) length of time in hospital, (c) after-effects of treatment to which children are extremely sensitive.

Method T.I.P., i.e. sodium tetrazodophenolphthalein (Shadocol or Opacol) was administered to 30 children and 3 adults suffering from amoebiasis. The acidic form is prepared for oral administration and represents a suspension of the white acid body which reverts to the blue soluble salt in the intestinal canal. The dye is absorbed from the intestine, secreted by the liver and excreted with the bile. No special dietetic measures or other medication were

employed. To children under six years of age half a bottle of the dye was administered and a full bottle to those over six years of age usually at night after a light meal. The next morning a dose of saline cathartic was given. Examinations of at least six fresh faecal specimens were made in every case beginning on the day after the saline purgative but it is fully recognized that further stool examinations over a longer period are desirable.

A table of 33 cases of amoebiasis shows that many of the patients had multiple infections with *Giardia*, *Ascaris*, *Trichuris trichiura* and *Taenia saginata* but these parasites were unaffected by the dye. Generally speaking symptoms attributable to amoebiasis abated and in 74 per cent both free forms of *E. histolytica* and its cysts disappeared. The authors very properly insist that the immediate purpose of this report is to stimulate interest and it is hoped that further trials will be made. The findings certainly merit further study to determine the exact therapeutic value of T I P in amoebiasis either as an immediate out patient treatment or as an ancillary treatment in hospitalized cases.

Philip Manson Bahr

BERTHO A. Pharmakologische Prüfung der Extrakte und Alkaloide aus *Holarrhena antidysenterica* [Pharmacological Tests of the Extracts and Alkaloids of *Holarrhena antidysenterica*] *Arch f Exper Path u Pharm* 1944 Mar 15 v 203 No 1 41-6 [Refs. in footnotes.]

The author has continued his earlier work to which reference is made in the paper under review on the alkaloids of *Holarrhena antidysenterica* (kurchi). He has carried out a series of toxicity tests on ciliates (colpidium and paramedium) and daphnia. The already known fact that the mixture of total alkaloids was more active than conessine suggested that one of the other alkaloids would be found to be more active. Accordingly, conessine-HCl, konkurchine-HCl, kurchidine-HCl, the mixture of crude alkaloids and two petrol-ether extracts (fractions A and B) were compared with emetine-HCl and quinine-HCl. If the activity of emetine-HCl is taken as the unit that of quinine-HCl and conessine-HCl is 4 and that of konkurchine-HCl is 8. This activity of konkurchine-HCl is greater than that of the total alkaloids or the extracts but it is evident that this activity will vary with the quantities of the highly active konkurchine present.

It is well known that the chemistry of the kurchi alkaloids is in a very confused state and until alkaloids of undoubted purity have been isolated biological results are likely to be contradictory. A full account of these alkaloids will be found in HENRY's *Plant Alkaloids*. C M Wenyon

WU C C Ya Tan Tzu Treatment of Amebic Dysentery *Chinese Med J* 1943 Oct-Dec. v 61 No 4 337-41

Ya Tan Tzu, the Chinese name for the seeds of *Brucea javanica*, was suggested by H L Liu as a new specific for amoebic dysentery in 1937. [Another name for these seeds is kô-sam. They had been used for treating dysentery in China since 1765 and Burroughs Wellcome & Co had a preparation of it on the market Tabloid Kô-sam in 1905, the drug was therefore not a new specific (see this *Bulletin* 1937 v 34 855).]

The author has been testing this drug again. The first six patients he treated according to Liu's dosage of 20-50 seeds but with disappointing results, one only giving a satisfactory response. He therefore increased the dose and

changed somewhat the method. His routine was a six-day course. On the first, third and fifth days 20 seeds in capsule were taken three times a day by mouth on the second fourth and sixth days 20 seeds were allowed to soak for two hours in 200 cc. of 1 per cent. NaHCO_3 and given as an enema to be retained after a wash-out. The effects were noted from the clinical aspect and repeated sigmoidoscopy gave information as to the healing of the lesions.

The author has thus treated 25 patients during the last 3½ years their ages ranging between 11 and 67 years 21 were males, 4 females. Ten were acute cases less than one month's duration, 15 were chronic, from several months to seven years duration. Mobile *E. histolytica* was found in every patient. In 19 of the 25 symptoms cleared in two to five days and the *Entamoeba* could no longer be found in the stools. The local lesions healed in 5-10 days in six patients and within another week in seven more. Three others were recorded as "improved" symptoms abated and the *entamoeba* disappeared but in one patient in poor condition the symptoms recurred three weeks later another a syphilitic feeling better refused further treatment the third suffered from bacillary dysentery also so the local lesions did not clear up till this, too had been treated. Three are returned as failures but in one of these the bowel symptoms cleared up though the fever continued, and a liver abscess was found and emetine given. Three of the first group were followed up. Five had remained well but had left hospital only 2-3 months another had been out 18 months, two others for more than two years and eleven for more than three years and had remained well. Two relapsed, three and six weeks respectively after discharge one of these was again successfully checked by Ya Tan Tzu.

Toxic effects were negligible eight patients complained of nausea and four vomited a few had abdominal discomfort or actual pain (but this may have been due to the dysentery and not to the drug) Ya Tan Tzu should certainly be given further trial and if reports continue to be satisfactory it should prove a valuable addition to the medical armamentarium for amoebic dysentery.

H. Harold Scott

KESSEL, J. F. ALLISON D. K. RADKE, Martha QUIROS, Maria & GLOECKNER, A.
The Cysticidal Effects of Chlorine and Ozone on Cysts of *Entamoeba histolytica* together with a Comparative Study of Several Encystment Media.
Amer J Trop Med 1944 May v 24 No. 3 177-83 2 graphs. [12 refs.]

In the tests carried out in the work described in this paper cysts of *E. histolytica* were added to a litre of water to a concentration of 100 cysts per cc. At the same time the bacterial concentration was 500,000 to 1,000,000 per cc. To the litre suspension which had been previously buffered to give and maintain the required pH, was added chlorine in the form of gas or calcium hypochlorite (H.T.H.) to give a residual chlorine concentration of 0.5 or 1.0 p.p.m. or ozone to give a residual ozone concentration of 0.1 to 0.3 p.p.m. All the experiments were carried out at a temperature of 27°C. while the organic nitrogen varied from 0.5 to 2.0 p.p.m. The time of exposure of cysts to the chlorine or ozone varied from 2 to 240 minutes, while the pH constant for each observation varied from 5 to 9. The cysts were obtained by first growing the amoebae in buffered liver infusion agar covered with buffered serum-Ringer solution. The amoebae were then introduced into the same medium to which starch had been added. Maximum encystment occurred within 60 hours. The sediment which contained the cysts was washed and centrifuged three times in distilled water the cyst suspension being finally stored in the ice chest. For each observation 100,000 cysts were added to a litre of buffered water.

The cysticidal times may be summarized as follows —

Cysticidal time in minutes at various pH values and various residuals

	pH 5	pH 6-8	pH 9
H.T.H. 0.5 ppm	30 mins.	120 mins	120 mins
Cl 0.5 ppm	30	60	120
Cl 1.0 ppm.	15	30	30
Ozone 0.3 ppm.	2	4	4

From the results obtained in tests carried out under the foregoing conditions the authors have reached the following conclusions —

1 Gaseous chlorine producing a residual of 0.5 p.p.m. when compared with H.T.H. producing the same residual was in general more active.

2 The activity of chlorine tended to decrease at the higher pH levels studied while the activity of ozone was less at pH 6 than at pH 5 but was not reduced between pH 6 and pH 9.

3 No great differences were noted between the bactericidal and cysticidal effects of the loads tested. It must be noted that the bacterial load tested was unusually heavy and if a bacterial load of 100 to 1 000 per cc. were tested the bactericidal times would have been lower.

4 The bactericidal and cysticidal times required by ozone producing a residual of 0.3 p.p.m. were several times less than those required by chlorine producing residuals of either 0.5 p.p.m. or 1.0 p.p.m.

5 A buffered liver infusion agar base with a buffered serum mixture is described as an encystment medium for *E. histolytica*. The results of cyst production on this medium are compared with cyst production on Boeck-Drbohlav's Ringer's-Egg Serum, Cleveland-Collier's Difco-Entamoeba Medium (2 per cent agar), Locke's Solution and Rice Starch and Chang's Buffered Liver Infusion Broth. In our hands the buffered liver infusion agar was superior in cyst production to the other media tested. [See also this *Bulletin* 1938 v 35 581 1936 v 33 532] C. M. WENYON

Hsu K. C. Human Intestinal Parasites in Northwest China. A Brief Survey
Chinese Med J 1943 Oct.-Dec. v 61 No 4 292-5

[5] RELAPSING FEVER AND OTHER SPIROCHAETOSSES

POLAKOW R. ORDMAN D. Relapsing Fever in Graaff-Reinet [Cape Colony]
S. African Med J 1944 Aug 28 v 18 No 16 271-5

The first part of this paper by Polakow comprises records of three military and six civilian cases of relapsing fever occurring in Graaff-Reinet in January and February 1944. In a footnote he mentions that *Ornithodoros moubata* had been found in the neighbourhood and also that the Public Health Department

had announced the presence of a widespread epidemic of 400 cases of relapsing fever in Graaff Reinet District, and several other areas in the Cape Province.

The second part of the paper by Ordman, comprises a record of an investigation of the relapsing fever position in the non-European population of the same district. An examination of the records at the Midlands Hospital from February 1941 to March 1944 gave a total of 120 patients with typical symptoms of relapsing fever and 63 possibles whose temperature charts showed suggestive readings. Blood smear examinations gave eight positive for spirochaetes in February 1944 and 18 in March in addition there were 17 and 13 cases respectively in these months which were negative but the results are not acceptable since the blood was taken without reference to the temperature of the patients.

Houses in the Graaff Reinet and Adendorp locations were found to be more or less infested with *Ornithodoros moubata* some of which were infected with relapsing fever spirochaetes. It is estimated that about 500 cases of the disease had occurred in the non-European population of the district in the last two years mainly in the six months ending March 1944. There is evidence that infected ticks are present on some of the farms. The disease is evidently endemic in Graaff Reinet and district and during the summer months may reach epidemic proportions unless measures are undertaken for the eradication of ticks.

E Hindle

SCOTT R. B. Neurological Complications of Relapsing Fever. *Lancet*. 1944 Sept. 30 436-8 3 figs. [12 refs.]

The campaign in the Libyan Desert yielded cases of relapsing fever of a type not previously known in Egypt, due to infection with a strain of *Spirochaeta recurrentis* transmitted by the bite of a tick resembling *Ornithodoros erraticus* [See this Bulletin 1942, v 39 846.]

The author saw a series of 41 cases of the disease acquired in the Western Desert nine of which showed nervous complications. These complications arose at various times during the illness but were more common after the third week. The nine cases are described in detail and fall into three categories (1) those with meningitis (2) those with signs of focal nervous damage and (3) those with both these symptoms. The cerebrospinal fluid was examined in eight of the patients and showed a lymphocytic pleocytosis with a total cell-count sometimes as high as 2,000 per cmm. Treatment with arsphenamine was ineffective. The prognosis was difficult, some cases showing repeated relapses though the majority recovered completely. There were no deaths.

E Hindle

GASPERINI, G. C. Considerazioni sulla epidemia di "Febbre Ricorrente" nei distretti di Asghed e Taellim Baet e Dombé Arrai (Tigrai Orientale) nell'ottobre-novembre 1940. [The Epidemic of Relapsing Fever in Tigrai, 1940.] *Boll. Soc. Italiana di Med. e Igien. Trop. (Ser. Entom.)* 1942, v 1 No. 3, 32-6

KANE, F. F. Rat-Bite Fever due to *Streptobacillus moniliformis*. [Correspondence.] *Lancet* 1944 Oct 21 348.

A case reported from N. Ireland.

PATTERSON H. M. Weil's Disease. A Report of Thirty-Seven Cases. *Hawaii Med. J.* 1944 May-June v 3 No 5 213-21

A report of 37 cases of Weil's disease in Hawaii all occurring among the Olan Sugar Company employees, which has had an average population of 5,200 during the past two years.

Thirty four of the patients were sugar cane-cutters and the disease occurred mainly among the male Japanese cutters below 24 years of age. The clinical picture was found to be characteristic though 57 per cent. in this series showed no jaundice. Repeated blood agglutination tests are considered to be the most reliable laboratory procedure for diagnosis.

The author recommends for treatment the use of whole blood transfusions from convalescent patients but only two patients seem to have been treated in this manner both with favourable results.

[See also this *Bulletin*, 1944 \ 41 577-8]

E Hindle

LEPROSY

BIESTRE MIYARES J J. Clasificación Sud-americana de la lepra [South-American Classification of Leprosy] *Trans Primera Conferencia Cubana de Leprologia Santa Clara Cuba Abril 1 y 2 de 1944* 13-21

A satisfactory classification of leprosy is important from the aspects of prognosis of treatment and of prophylactic control. Leprosy being especially prone to attack the skin and peripheral nerves (though other tissues and organs of course do not escape) it has been and is customary to divide cases into cutaneous neural and mixed. The author while not criticizing this classification is all in favour of the following on an anatomico-pathological basis (1) Lepromatous (2) Tuberculoid (3) Non-specific. He details the characters of each of these from the aspects of (i) Pathological anatomy (ii) Clinical features (iii) Bacterioscopy (iv) Immunology. The first is characterized by lepromata and infiltrations crowded with bacilli. It is highly infective and of severe type anergic giving a negative Mitsuda reaction. It does not as a rule in the early stages at all events affect the general health and the patients can do quite heavy work but they must be segregated either in their houses or in colonies under supervision and strict hygienic conditions. They do not respond well to treatment by chaulmoogra.

The second type is in many respects the converse of the first. These patients present reddish discolorations sometimes raised or merely macular with infiltrated borders and small nodules micropapuloids the lesions are follicular limited and contain few bacilli corpuscular sedimentation is within normal limits the lepromin test is usually positive the body is putting up a good resistance these patients are not contagious they can carry on work with their fellows and with certain precautions can live at home they respond to chaulmoogra treatment and may be cured.

The third non-specific type presents achromic patches or level erythematous maculae varying in number slightly if at all infiltrated with definitely marked edges the peripheral nerves are enlarged and indurated. In this form one sees the *main-en-griffe* the perforating ulcer bone absorption etc. Whereas it is rare for the malignant lepromatous form to become the benign tuberculoid there are three possibilities for the third type. It may remain true to itself or may pass over to either of the other two. The nasal mucus and the skin lesions show bacilli in about half the cases the lepromin reaction is positive in about the same proportion (some say 60 per cent.) If the hygienic surroundings are good, the diet adequate qualitatively and quantitatively and treatment be persisted with the outlook of these cases is favourable.

H Harold Scott

ISARRA, R. Censo de lepra. [Leprosy Census.] *Trans. Primera Conferencia Cubana de Leprologia Santa Clara Cuba Abril 1 y 2 de 1944* 33-8 1 fig.

DOMÍNGUEZ LÓPEZ, F. Censo de lepra en Camagüey. [Census of Leprosy in Camagüey.] *Trans. Primera Conferencia Cubana de Leprologia Santa Clara Cuba Abril 1 y 2 de 1944* 39-43

DE CASTRO PALOMINO, J. Lección de clínica sobre lepra. [Address on Clinical Cases of Leprosy.] *Trans. Primera Conferencia Cubana de Leprologia, Santa Clara Cuba Abril 1 y 2 de 1944* 22-32, 5 figs.

This is a record of a clinical address at which the author showed about 75 coloured photographs of cases of the lepromatous, tuberculoid and "non-specific" types of leprosy. The letterpress is very elementary and more of the nature of a lecture to students. There are good illustrations of the three types but otherwise the article is hardly up to the standard of a Congress paper.

H. Harold Scott

COT LESMES, V. El toxoide diftérico en el tratamiento de la lepra. [Diphtheria Toxoid in the Treatment of Leprosy.] *Trans. Primera Conferencia Cubana de Leprologia Santa Clara Cuba Abril 1 y 2 de 1944* 44-51

The first part of this paper is concerned with relating the work of COLLIER, OBERDORFFER, MCKEAN and FAGET and JOHANSEN and their results from the use of diphtheria toxoid in leprosy. Publications by all these have been abstracted in this Bulletin (1941 v 33 28 704 1942 v 39 231 232, 462, 697 698). The author goes on to report the results obtained by him in 63 patients. His results are of special interest because they show fundamental differences from those obtained by MCKEAN [this Bulletin 1942, v 39 231 and see TIAS below]. The author intended to report on 100 patients but 37 received less than six doses or did not return for observation and the results in their cases could not be checked. The rest received 6-10 injections at least four had 33-36 in 14-28 months and one had 42 in 20 months. Observation has been kept up in some cases for "a long period" and in one for less than a year. He modified COLLIER's technique, injecting 0.25 cc. as an initial dose repeating the injection every two weeks in gradually increasing doses to a maximum of 3 cc. and then reducing to 1.0 cc. In some in order to test the patient's susceptibility the first dose was 0.1 cc. then increased by 0.1 cc. every three days till the larger doses were reached. These were given as with the others every other week. Later after this method had been in use for 18 months the patients received an injection every week up to a maximum of 1.0 cc. and this was maintained unchanged, except for two patients who developed an abscess each time this dose was given and they were therefore given only 0.1 cc.

Of the 63 there were 29 of the lepromatous type. Of these 16 improved, 12 remained stationary and one was worse. Twelve were of the tuberculoid type and of these two improved, nine were stationary and one continued to get worse. Of 22 non-specific cases 10 improved, 11 were stationary and one worse. If percentages may be permitted to point out the differences with so small totals 55 per cent. of the lepromatous improved, 16 of the tuberculoid and 45 of the non-specific. The verdict "improved" was given if "all or most of the lesions disappeared the rhinitis cleared and sensation returned the patient gained in weight, and his general health was bettered." All the author's patients were going about and followed their usual way of life. With a chronic disease subject to periods of remission and exacerbation it is obviously

difficult accurately to assess the value of a special form of treatment but the author notes particularly the greater proportion of improved among the lepromatous cases among whom we saw truly spectacular results. In six of them (four were advanced L3 cases) the lesions were so changed that patients who a short time before showed large lepromata and infiltrations of face ears and other parts of the body would no longer be regarded as lepers. [Compare this with McKEAN's verdict that treatment with diphtheria toxoid proved to be of no value in either major tuberculoids with numerous bacilli or in the papular type of lepromatous cases and even active minor tuberculoids free from bacilli failed to respond (this *Bulletin* 1942 v 39 231) see also TIAN below]

H Harold Scott

TIAN F R. Tratamiento de la lepra [The Treatment of Leprosy] *Trans Primera Conferencia Cubana de Leprologia Santa Clara Cuba Abril 1 y 2 de 1944* 52-63

A candid statement of the author's views and a general summary of present day knowledge of the treatment of leprosy. 'Leprosy is not incurable' he says any more than is pulmonary tuberculosis. As nobody would pretend to cure a man weak in poor surroundings and with a tuberculous cavity so we cannot hope to restore to social life a leper with advanced bacillaemia and cachexia. In the curable stages confidence constancy and perseverance in treatment are necessary. He tells how one vaunted remedy after another is brought forward only to fall back into obscurity. He mentions methylene blue mercurochrome fluorescein gold iodide of potassium vaccines antiserum and others. Diphtheria toxoid which gave such great hopes after the sensational reports of Collier appears already condemned to oblivion through its failure in the hands of nearly all leprologists [but see COT LESLIES (above)]

The author then enumerates and considers certain fundamental principles namely (1) Whole-hearted co-operation of the patient (2) Raising the patient's resistance and his general state of health by exercise proper food etc. (3) Specific treatment (chaulmoogra oil) in as high a dosage as the patient can tolerate without upsetting his general health (4) Uselessness of persisting with treatment in burnt out cases

He then considers in more detail the use of chaulmoogra the preparation dosage route of administration intravenous intramuscular subcutaneous and intradermal (la plancha method) the last of which he urges. Progress of treatment must be controlled by noting the temperature the weight blood sedimentation any leprous reaction

H Harold Scott

HELMINTHIASIS

OLIVER-GONZÁLEZ J & TORREGROSA M V. A Substance in Animal Parasites related to the Human Isoagglutinogens. *J Infect Dis* 1944 May-June v 74 No 3 173-7 [13 refs]

1 Following the method outlined by Melcher and Campbell a polysaccharide fraction has been isolated from the dried and pulverized material of the following helminths *Ascaris suum* *Ascaris lumbricoides* *Trichinella spiralis* *Necator americanus* *Schistosoma mansoni* and the larval form of *Taenia solium*. When added to human serum all polysaccharide fractions inhibited the α and β agglutinins in the serum. They also inhibited the hemolysis of sheep cells in a system consisting of Forssman antiserum sheep cells and guinea pig complement

"2. A high titer of the α agglutinins has been detected in the serum of a small number of malaria patients belonging to Groups O and B who had suffered repeated attacks of the disease.

3. The relations that may exist between parasitic infections and the autoagglutination of erythrocytes as a result of the immunization of the host by a substance in the parasite related to the isoagglutinogens are herein discussed.

BRUCE R. C. Bilharzia Disease some Prevalent Misconceptions. *South African Med J* 1944 July 22, v 18, No. 14 239-41

This article has much the same contents as one published by the author in 1942 [this Bulletin 1943 v 40 550]. In the course of his work as a urologist in Johannesburg, South Africa, he has been much impressed by the number of cases of urinary schistosomes which could only be diagnosed by cystoscopy. About 75 per cent of some 130 cases seen by him during the last three years had to wait for five to twenty five years before Bilharzia was diagnosed. He discusses the symptoms and signs of the disease and its treatment. Probably at least 80 intramuscular injections of 4 cc. of antischistosomal or founadin are required for an adult and 150 cc. of Fantom intravenously. If possible the result should be checked by cystoscopy.

The author concludes that cystoscopy is the only reliable method of diagnosing the infection.

J F CORSON

SILVEIRA, J. A localização pulmonar da esquistossomose americana. *América Pulmonary Schistosomiasis. Rev 4ma Med Argentina* 1944 June 9 v 55 No 536 444-7 [14 refs.]

This is a general account of pulmonary schistosomes due to *Schistosoma mansoni* which is the author thinks commoner than is generally realized. He compares his findings with those of SHAW and GHAREEB [this Bulletin 1938 v 35 665] who studied pulmonary schistosomes due to both *S. mansoni* and *S. haematobium*. While Shaw and Ghareeb found pulmonary lesions 33 per cent of 282 autopsies, KORNISCH [this Bulletin 1942, v 39 563] studied 147 cases (10.8 per cent.) Silveira explains this difference in the incidence reference to the fact that *S. haematobium* has easier access to the lung by way of the vesical plexus and internal iliac vein (it reaches the lung in 50 per cent cases) while *S. mansoni* has more difficulty in reaching the lung (by way of porto-caval anastomoses). This is confirmed by the observation that cirrhosis affects but little the migration of *S. haematobium* to the lung, is decisive for *S. mansoni*.

Pulmonary schistosomes caused by *S. mansoni* alone exists always the migration of the larvae through the lung. This constitutes the toxic form of the disease, which can be fatal without being recognized. The chronic form is due to the arrival of the adult worms in the lung. Clinically there are two forms of the disease, the pulmonary form with respiratory symptoms (e.g., bronchitis) and the vascular form due to embarrasement of the lung circulation resulting arteriolitis, alveolitis, obliterating arteritis and similar changes can be formed which may be other conditions e.g., bacillary tuberculosis. Nodules may be seen on the pleural surface of the lung and subpleural lesions may be seen in eggs or adult worms. The author refers to two cases in which pneumothorax was probably due to schistosomiasis. The

conditions are similar to those described by Shaw and Ghareeb. The only certain diagnosis is by finding the eggs in the sputum. Failing this diagnosis must be made on the results of examination of the faeces: the intracutaneous test, the eosinophilia provoked by the administration of antimonial compounds [see MAINZER this *Bulletin* 1937 v 34 394] the clinical signs, the epidemiological conditions and the results of treatment. Radiological signs are not characteristic. There may be shadows of the nodules which may be miliary and are then easily confused with other conditions (e.g. miliary tuberculosis) intensification of the general picture of lung structure and changes at the hila and in the pulmonary artery due to circulatory embarrassment. The cardio-vascular bronchitic and other secondary symptoms must be treated as well as the general infestation for which antimonial compounds are recommended.

G Lapage

BERCOVITZ Z T RODRIGUEZ MOLINA R. HARGRAVE D W DICKIE J D & GREEN C E Studies on Human Schistosoma Mansonii Infections. I. Proctoscopic Picture in Asymptomatic Schistosomiasis Mansonii Infections. *J Amer Med Ass* 1944 Aug 5 v 125 No 14 961-3 3 figs

In the routine examination of army recruits in Porto Rico [West Indies] ova of *Schistosoma mansoni* were found in the faeces in about 10 per cent. A proctoscopic examination was made in 155 of these infected young men and small ulcers were found in 94. The ulcers were only a few millimetres in diameter, some were linear and others of pin point form, and they were sharply demarcated from the surrounding normal mucosa, with no signs of inflammation. They were nearly always lying directly on the capillaries or at their bifurcation and were situated below the recto-sigmoid fold. Reference is made to the investigations of KOPFISCH [this *Bulletin* 1942 v 39 563, 1943 v 40 703] in Porto Rico. The authors conclude from this examination that in areas where the presence of *S. mansoni* is suspected careful examination of the faeces should be made regardless of the absence of any signs or symptoms of the disease.

J F Corson

DI GIACOMO M P & MAYER R A Schistosomiasis mansonii. *J Amer Med Ass* 1944 July v 125 No 13 904

Two cases of infection with *Schistosoma mansoni* are reported. Both patients were Arabs and were treated at the U.S. Marine Hospital, Ellis Island, New York, in September and October 1943. The first case presented no unusual features but the second patient, who had lived in the United States for the past 20 years, complained only of low back pains, weakness and some loss of weight during the last two years. He had received various forms of treatment for lumbosacral strain without effect. Ova of *S. mansoni* were found in the faeces and he was treated with Fuadin [Fouadin or Neocantimosan, Bayer, stibophenem B.P. Add III] and cured.

The authors remark on the insidiousness of this disease and recommend that anyone who has returned from an endemic area should have a stool examination for the ova, whether he has symptoms or not.

J F Corson

PIÑA DAZA M Algo mas sobre Schistosomiasis Mansonii. [More Facts about Schistosomiasis Mansonii.] *Bol Hospitales* Caracas, 1944 Jan.-Feb v 43 No 1 23-46 [13 refs]

This is a doctorate thesis on orthodox Spanish lines. The author deals with haematemesis in the latest stages of atrophic cirrhosis of the liver resulting from infestation with *Schistosoma mansoni*. He divides his work into the

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following sections (1) Haematemesis and its differential diagnosis [as found in elementary text-books of medicine] (2) Brief remarks on Banti's syndrome and Laennec's cirrhosis of the liver (3) Pathogeny of haematemesis in these conditions, especially oesophageal varix. In this section the author divagates to describe the surface anatomy and topography of the normal spleen, its nerve and blood supply and the way in which portal obstruction may cause haematemesis (4) Indications of the lines along which treatment may be directed [without details. There is a table giving some of the features of 18 cases. The first word of the title would not seem to be justified.]

H Harold Scott

KAMMER, V. Fever in *Ascaris duodenalis* [*Necator americanus*] Infection on the Upper Zambesi. A Review of 83 '932 Cases. *East African Med. J.* 1944 July v 21 No 7 218-20 1 chart.

An African native of Northern Rhodesia, aged about 25 years strongly built and well nourished, was admitted to hospital complaining of slight pain in the left upper part of his abdomen probably of about one month's duration. He was not anaemic and no other symptoms or signs of disease could be found on examination. His blood, urine and faeces were examined with negative results. His temperature rose to 100°F on the evening of the day of admission and again on the morning of the 4th day, then it fluctuated between 100°F in the mornings and 103°F (gradually falling to 101°F) in the evenings until the 10th day after which it remained normal. On the 8th day eggs of *Necator americanus* were found in the faeces a dose of 60 minims 1/4 cc of carbon tetrachloride followed by magnesium sulphate was given on the ninth day. The temperature fell and the pain completely disappeared.

The author examined the records of 832 cases of hookworm [*N. americanus*] infection in the same hospital during the period 1937-1942 less than 1 per cent. had any accompanying fever and in such cases the temperature lasted only for about two days and was usually about 100°F. Among various possible causes of fever in this case, an allergic reaction due to previous hookworm infection is considered solely with *Necator americanus* the name *Ascaris duodenalis* appears only in the title, an obvious slip, as is also the number for 832.

J F Corson

FLEMING A. McK. A Case of Intractable Diarrhoea and High Eosinophilia due to Hookworm. *East African Med. J.* 1944 July v 21 No 7 221-2.

This is a report of a case of hookworm infection in a European acquired, apparently by a single exposure of short duration. Mr X and his wife taking a walk along the sea shore north of Mombasa, Kenya Colony on July 3rd 1943 came to a muddy stream, about 10 yards wide, and removed their shoes and waded across. Mr X stood in the water for a few minutes while his wife waded straight through. Four days later Mrs X developed itching and redness of the left foot and on the following day her husband had a similar but more severe eruption on his right foot consisting of a "mass of red pimples in diameter" sole and outer side of the foot, each two or three millimetres in diameter. The pain and eruption gradually subsided within the next 10 days. On July 27th he complained of slight nausea, headache, lethargy and irritating cough. Examination of his blood and urine was negative. On July 31st he had a sudden attack of diarrhoea and during the next month he suffered from colic, extreme flatulence and watery diarrhoea with 2 to 12 motions per day. His abdomen was usually distended and flatulent, and tender in the umbilical

region. His appetite was fair and he had no nausea or vomiting but lost 16 lb in weight. All medicinal treatment failed to relieve the condition. The faeces were examined eight times between August 4th and 31st without result but on September 1st—59 days after the seashore walk—scanty ova of hookworm were found and he was then treated for hookworm infection. On August 27th his blood showed 17,200 leucocytes per cmm. and 40 per cent were eosinophiles the erythrocyte count showed 4 720 000 per cmm.

Gradual improvement followed it was necessary to give six treatments with oil of chenopodium and carbon tetrachloride and even at the time of writing [May or June 1944?] hookworm ova were sometimes found in the stools. On May 11th 1944 a differential blood count showed eosinophiles 11 per cent Mrs A also became infected but had no symptoms and was promptly cured by two treatments [The species of hookworm in this case is not given. Infection following one exposure is recorded by ASHFORD in The Practice of Medicine in the Tropics by BIAN and ARCHIBALD 1923 v 3 1849]

ALLEN H C. Eosinophilia in the South Pacific. U.S. Nav Med Bull 1944 June v 42 No 6 1241-4 1 chart. J F Corson

At a base hospital in the South Pacific 17,502 differential leucocyte counts were made between June 1942 and September 1943 in 897 of the blood films there were over 10 per cent of eosinophils. The proportion of patients with eosinophilia among hospital admissions increased more or less steadily from 1.4 per cent in June 1942 to 20.3 per cent in September 1943. This is shown by curves which give the figures for army navy and marine personnel and show that the increase occurred in all three branches. It was suspected that the eosinophilia was caused by helminth infestation and in August 1943 as patients were then being kept in hospital longer than before greater attention was paid to stool examinations. In this month 139 patients had eosinophilia of over 10 per cent. In 71 the faeces were examined and in 30 helminth infestation was found. 28 had hookworm 1 had *Strongyloides stercoralis* and one had both these infestations. During the whole period of 16½ months 16 patients had an eosinophilia of over 50 per cent. hookworm ova were found in eight *Strongyloides stercoralis* in one and both infestations in one. The author thinks that a large part of the eosinophilia was due to hookworm infestation.

ENGEL R. Geheilte Strongyloides stercoralis-Infektion [An Instance of the Cure of an Infestation with *Strongyloides stercoralis*] Deut med Woch 1944 Mar 31 v 70 No 13/14 188-9 J F Corson

The author briefly reviews the records of strongyloidiasis in Hungary. No references are given but these records include an epidemic of 38 cases in a nursery school in Budapest in 1926 and an infestation of a man aged 21 in 1928. LÖRINCZ found the larvae of this species in nine cases (0.6 per cent of all the subjects whom he studied) when the stools were systematically examined. He found these larvae in different regions of Hungary but they were more often present in the provinces than in Budapest and were more frequent in males under 15 than in older people. von Engel describes one case found in Kassa where the infestation has not hitherto been recorded. The patient was a woman aged 28 she had lived in the Kassa region since 1929 except for a visit to Budapest lasting six weeks. She had never been seriously ill and had suckled her third child. Her illness began with a marked stitch at the right costal border followed by repeated severe cramps. There was irregular fever (39-40°C) perspiration and variable appetite. The stools were normal. The

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patient was very nervous. There was no jaundice but bile pigment was found in the blood. Four days after treatment for inflammation of the gall bladder the temperature was normal and the pain and tenderness in the liver region had disappeared. But duodenal intubation revealed larvae of *Strongyloides stercoralis* in the bile. In bile A and B there were 70-80 larvae but there were few in the thinner bile C. No eggs were found in either the bile or the stools. Isolated larvae were found in the stools and more were found after purgation. The patient could not remember any skin eruption. The stools of her husband and children were negative. The origin of the infestation was not traced.

After treatment of the anaemia the author unsuccessfully tried sulphaguanidine, acridin carbon tetrachloride, Lubisan (a resorcinol compound, Bayer Products) and filix mas with thymol. Lubisan decreased the number of larvae from 70-80 to 5 or 6. Intravenous neosalvarsan also reduced the number of larvae. Gentian violet was then tried. On the first day 250 cc. of a 1 per cent. solution were introduced into the duodenum in quantities of 50 to 60 drops per minute. The patient reacted badly with continuous retching, some 100 cc. of the gentian violet were found in the duodenal contents. The next day, 5 or 6 larvae were found in the duodenum. On the fourth day the patient was then given only 100 cc. at a slower rate. On the fourth day there were no larvae. On the fifth day 50 cc. and on the sixth day 100 cc. of the gentian violet solution were given. No larvae were found after this and none was found a week later in either the stool or duodenal contents. (Kraso & Faust (Clinical Parasitology 1943 p. 254) state that viable larvae may be passed for days or weeks after the completion of the course of treatment with gentian violet which they describe, but that the parasite females may subsequently die. cf also SUTCHIKOVA and SEMENOVA, this Bulletin 1944 v. 41 411. LEVIN *ibid* 411 and LOWE and LANCASTER, *ibid* 851.)

G. Lafay

KASIMOV B. [First Case of *Ostertagia ostertagi* in Man in Azerbaijan.]
Med. Parasit. & Parasitic Dis. Moscow 1943 v. 12 No. 5 81 [In Russian.]

The author found in the small intestine of man at autopsy one specimen of *Ostertagia ostertagi* (Stiles 1892) [presumably *Ostertagia ostertagi* (Stiles 1892)] and one specimen of *Trichostrongylus colubriformis* (= *Trichostrongylus instabilis*). *Ostertagia ostertagi* [normally in the fourth stomach of cattle as a sheep] has not been recorded before from man. [*T. instabilis* has been recorded as an occasional parasite of man.]

Kasimov describes the specimen of *Ostertagia ostertagi* found by him as follows:—

Length 8.9 mm. with a maximal width at region of the buccal papillae of 0.111 mm. Width at the region of the cervical papillae 0.042 mm. at the posterior end of the pharynx 0.051 mm. and at the level of the excretory pore 0.038 mm. Pharynx 0.579 mm. long with a maximum width at the point of transition to the intestine of 0.042 mm. Excretory pore 0.321 mm. from the head end. Cervical papillae 0.343 mm. from the head end. Dorsal ray of the bursa 0.064 mm. long bifurcating into two branches at a distance of 0.047 mm. from its base. The two secondary branches again divide into two hardly noticeable twigs. The dorsal ray reminded the author of the dorsal ray of *Ostertagia gricikera* parasitic in the remdeer (see SEMENOV 1937 *ibid* 108). Spicules equal golden in colour 0.214 mm. long with a maximum

width 0.021 mm with truncated distal ends forming thick branches and two thin branches. Gubernaculum grey in colour narrowing at the distal end 0.060 mm. long and 0.012 mm wide at its distal end [cf. KASIMOV this Bulletin 1943 v 40 323 in which paper the author records the finding in man of *Ostertagia circumcincta*. It is not clear from the account of the specimen of *O. ostertagi* given in this paper whether the specimen found was actually parasitic or merely a passenger in the human intestine. Theoretically it would be possible for isolated specimens of this species or of *O. circumcincta* to survive in the human intestine for a while after the ingestion of uncooked or partially cooked abomasum of cattle or sheep or goats. *Ostertagia ostertagi* especially might be so ingested because it occurs in nodules in the abomasum. Both species are adapted to life in the acid environment of the fourth stomach of the ruminant and not to the alkaline environment of the human small intestine.]

GURL, R. Ueber Ascariasis der Gallenwege. [Ascariasis of the Bile Ducts] Schweiz med Woch 1944 June 3 v 74 No 22 600-605 3 figs (26 refs)

Human ascariasis has increased enormously since the end of the last war. Suggested causes of this increase are more vegetables, salads, fruit and uncooked food are consumed more people grow their own supply of vegetables and manure them with human excreta. malnutrition and lack of soap with consequent uncleanliness possibly also contribute in addition most carriers of *Ascaris* are unaware that they have the parasite. it is usually harmless but its effects may be fatal.

The author describes two cases in detail. One was a woman aged 47 with a history of vomiting and periodical colic in the right upper abdomen for five or six years. Treatment given six years before had evacuated 60 ascars. Further treatment six days before admission to hospital had evacuated three ascars. Previous treatment had removed 30 gallstones. The patient died after the onset of circulatory collapse. There was no icterus of the skin. The leucocyte count was 11 600 (neutrophils 90.5 per cent eosinophils 0.5 per cent). At autopsy 20-30 ascars were found in the liver and bile ducts two in the stomach 20-30 in the duodenum and ileum and two in the colon. The liver was enlarged 8 cm. beyond the costal border. The intrahepatic bile ducts were markedly dilated and one or more ascars protruded from these. The liver also found in them in sections of the liver. The hepatic bile ducts were four ascars there were none in the gall bladder or cystic duct. The central lobular veins were tightly packed with nucleated cells. There was interstitial hepatitis with cellular infiltration (lymphocytes neutrophils and eosinophils) which was especially dense around the bile ducts where eosinophils were numerous. The heart muscle showed brown atrophy some fatty degeneration and subendocardial haemorrhages.

The second patient was a woman aged 71. She had pain in the liver region and upper abdomen and marked skin icterus. There was no history of ascariasis but eggs of *Ascaris* were found in the stools and in A and B bile obtained by duodenal intubation. Symptoms of cholangitis and peritonitis developed and the patient died. The liver was enlarged three finger breadths. There was marked bilirubinuria and leucocytosis of 28 400 (neutrophils 91.5 per cent with a marked shift to the left but no eosinophils). Autopsy disclosed a subphrenic abscess. The much dilated duodenum contained five ascars. one of these was halfway up the ductus choledochus which was the size of the index finger. Some centimetres below its exit from the liver the duct was occluded by a yellowish brown stone (2½ x 1 cm.) between this and the wall of the duct was a

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dead, crumpled *Ascaris* (fig 3). The cystic duct was occluded and the gall bladder shrunken and embedded in cicatricial tissue. In the liver under a fibrous crust there were numerous yellowish, solitary or grouped abscesses, mostly composed of neutrophils and surrounded by hyperaemia. These were all near the markedly dilated bile ducts around which there was considerable overgrowth of connective tissue and inflammatory change. The liver capillaries were much dilated and the liver parenchyma brownish-red atrophic and atonic. The duodenal mucosa was hyperaemic, swollen and covered with tough mucus.

The author discusses at length the literature and the features of his two cases. In Europe, he says, women are most often affected in Japan the men. In the bile ducts *Ascaris* is most often found in the ductus choledochus. Its effects may be mechanical (dilatation of the bile ducts etc. lesions of their mucosa, promotion of the flow of bile by their movements) reflex (colic, etc.) anaphylactic or bacterial infection may result. Their toxins may perhaps cause biliary cirrhosis. Worm nodules under the capsule of the liver may be mistaken for carcinomatous metastases. No anthelmintic is known which will affect the ascarids in the bile ducts into which drugs may drive them deeper. The killing of them in these ducts may have dangerous toxic or infective results. Surgical removal of all ascarids from the intestine are recommended. If the ascarids are very deep massage of the liver may help their removal or they may be sucked out through a tube connected to a water pump. Ascarids may escape through drainage tubes in the ductus hepaticus or ductus choledochus. In one case recorded by FISCHER (no reference is given) 51 ascarids escaped in this way. G. Lapege

SCHNELLER G B & YOUNG R M. Clinical Studies on Microfilarial Periodicity in War Dogs. Bull US Army Med Dept. 1944 Sept. No 80 52-8 4 charts.

Observations were made on the periodicity of the microfilariae of *Dirofilaria immitis* in 54 infected dogs. The blood of four dogs was examined two-hourly from 8 a.m. to 9 p.m. the microfilariae being counted. The method used was to take 2 cc. of blood from the radial vein allow it to clot, remove the serum and examine 0.1 cc. of the serum spread out on a microscope slide. The numbers of microfilariae rose from 8 a.m. to 1 p.m. to a moderate height, fell somewhat to 3 p.m. then rose sharply to a maximum for the day at about 4.30 p.m. and again fell, somewhat rapidly to 7.8 or 9 p.m. This periodicity pattern was much the same in all the other dogs. As the pattern was different from those of other authors, the time of the chief rise was changed from 3 p.m. to 11 a.m. for a few days. This was followed by changes in the periodicity pattern varying in different dogs but the authors think that the patterns might have shown greater uniformity if the new feeding time had been continued for a longer period. Exercise appeared to have no influence on the counts. The results suggested that the spleen might be a reservoir for microfilariae. After ligation of the splenic artery in three dogs the microfilarial count in the peripheral vessels (radial and jugular veins) was higher than before ligation. The same occurred within five minutes after an intravenous injection of epinephrin hydrochloride. Splenectomy in two dogs was followed by a higher afternoon count of microfilariae. When epinephrin was injected into the splenectomized dogs the effects, if any on the microfilarial count were irregular.

The authors concluded from their investigation that microfilariae did not appear in the blood until about eight months or more after exposure of the dogs

to infection [See also this *Bulletin* 1935 v 32 277 1936 v 33 132 133 595 1938 v 35 385 1939 v 36 155] J F Corson

FOGEL, R. H. & HUNTINGTON R W Jr Genital Manifestations of Early Filariasis. *U.S. Nav Med Bull* 1944 Aug v 43 No 2 263-70 •

The early signs of filariasis *viz.* lymphangitis and lymphadenitis [called *mumu* by the natives of Samoa see BUXTON this *Bulletin* 1929 v 26 436] was found to be very prevalent among the American marine and naval personnel stationed in the South Pacific Islands. No microfilariae were found in the blood or tissue fluids although a high percentage of the adult natives showed blood infection. The chief insect vector of the infection was *Aedes scutellaris* (*variegatus*).

The lesions of *mumu* or acute filariasis were of two kinds (1) a persistent nodular lesion around an adult worm or its remains (2) a transient diffuse lymphangitis presumably due to sensitization. The latter formed most of the manifestations and it was common for both the genitals and one or more extremities to be involved. It was not associated with bacterial infection. In some cases there were swellings of the areolar tissue obviously allergic and probably of the same nature as Calabar swellings [though of different origin].

Constitutional symptoms—Fever was uncommon but headache vertigo blurring of vision and nausea were severe in some cases and muscle pain and spasm and chest pain were common.

Pathology—Genital tissue was available in two cases only. In a man with filarial funiculitis who died of coronary disease MICHAEL (personal communication) found diffuse oedema with lymphocytic and eosinophilic infiltration of the cord but there was no anatomical obstruction in the epididymis or vas deferens. In the other case an epididymo-vasectomy was performed and a similar condition was observed.

Physical signs—The following were seen (1) swelling and oedema of the spermatic cord the earliest and most characteristic sign (2) orchitis or hydrocele (3) epididymitis (4) vasitis (5) hydrocele (6) oedema of the scrotal skin (7) inguinal adenitis.

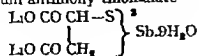
Three patients worked in the hospital and could therefore be closely observed. When the abdominal pain began the spermatic cords were not swollen but within 12 hours there was a palpable swelling high up in the inguinal canal. This gradually extended down the cord and at 24 hours the external abdominal ring was swollen and tender and within the next 24 hours the swelling had reached the scrotum. Scrotal oedema when present was always on the side where funiculitis existed but was not related to inguinal adenitis.

In differential diagnosis early filariasis must be distinguished from appendicitis, hernia and varicocele of non filarial origin. It is easily distinguished from the epididymitis of gonorrhoea.

Treatment—No drugs that were tried had any good effect. Rest in bed with scrotal support was beneficial. Operations on hydrocele, hernia and varicocele are contra indicated. [See also this *Bulletin* 1944 v 41 303 304 599 600 860] J F Corson

BROWN H W The Treatment of Filariasis (*Wuchereria bancrofti*) with Lithium Antimony Thiomalate. *J Amer Med Ass* 1944 Aug 5 v 125 No 14 952-8 3 charts [Refs. in footnotes]

Anthionalline is lithium antimony thiomalate



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A review is given of previous work about anthiomaline in the treatment of filariasis. Two reports (CHOPRA & RAO and HAWKING, this Bulletin 1940 v 37 858 1941 v 38 151) state that it had little effect in reducing the number of microfilariae (if *Donofilia*) in the peripheral blood. The author and his colleagues found it effective against *Onchocerca* in dogs.

The present work concerned 12 patients in St. Croix, Virgin Islands who were admitted to hospital for some other cause than filariasis. Microfilariae were present in the blood. In the case of adults anthiomaline 180 mgm. (3 cc.) was injected intramuscularly daily beginning with a half dose on the first day. Blood was taken from a vein at 10 p.m. for counts of the microfilariae. The number of microfilariae in control untreated patients remained constant for the six months period of observation. The course of the drug usually lasted 13-26 days the total quantity given being usually about 18-50 cc. The patients were observed for four to five months following the treatment.

Twelve patients received a full course of treatment in a thirteenth the treatment had to be abandoned after the first dose on account of asthmatic attacks. In one person there were no microfilariae in the blood, but the femoral and inguinal lymph glands were enlarged. There was no immediate response, but five months later he reported that the glands were no longer painful on exercise. In the other eleven cases at the end of treatment the microfilariae were more numerous in two cases and much less numerous in nine cases. After four to five months, the number of microfilariae was unchanged in one case and greatly diminished (85-100 per cent) in the other ten.

As regards toxic reactions vomiting and epigastric pain occurred in 40 per cent. (presumably 5 of the patients especially towards the end of the course. Local reaction at the site of injection was absent in most patients although firm intramuscular painless masses often developed. Fever occurred in two patients towards the end of treatment. Arthritic pains occurred in one case. There was no evidence of renal damage. Six patients developed transitory rashes which did not spread although treatment was continued. No pathological changes due to the death of the adult worms or of the microfilariae were observed. Anthiomaline is not the ideal drug for the treatment of filariasis but the results indicate that further investigations of its value should be made.

F. Hawking

WETZEL, R. Onchocercosis. Biopsy as an interpretation clinic. [Biopsy and its Clinical Interpretation in Onchocercosis.] *Medicina*. Mexico 1944 July 10 v 24 No. 463 285-73 8 figs.

The author describes the technique of biopsy for the diagnosis of onchocercosis. Biopsy of skin of the face or neck is usually most favourable because most nodules occur in these regions but the microfilariae may be found a long way from the nodules from which they originate, e.g., in the foot from nodules in the trochanteric region or even further away [see also WETZEL, this Bulletin 1944 v 41 305]. They may also cross from one side of the body to the other. They can be found in the subcutaneous tissue. Biopsies may be negative because the nodules contain nematodes which are immature or females which are mature but are unfertilized, or fertilized females which have not yet produced larvae, or larvae which have not yet left the nodules. Biopsies may be positive when inspection of the skin reveals nothing abnormal whether there is a history of onchocercosis or not [see this Bulletin 1923 v 20 845]. Other types of case are —

1. Patients with oedema of some region increase of local temperature and indurated skin. This occurs most often on the face, shoulder arm forearm and

hand and is known locally as coastal erysipelas. Biopsy is negative or microfilariae are scanty.

2. Patients in whom inspection shows abnormality of some region of the body. The skin is thickened and has an olive green colour but the local temperature is normal. Biopsy reveals numerous microfilariae. The skin of the ears, nose and cheeks is most often affected and the disease is locally known as purple disease (mal morado).

3. Patients with the onchocerciasis facies who have been parasitized for several years. They look prematurely old and biopsy reveals numerous microfilariae all over the body.

G Lapage

MAZZOTTI L. & LOZANO HUBE Elena. La prueba intracutanea de Bachman para el diagnostico de la triquinosis en 1 000 personas sanas de la ciudad de Mexico. [The Diagnosis of Trichinosis by the Bachman Intracutaneous Test in 1,000 Healthy Persons in the City of Mexico.] *Rev Inst Salubridad y Enfermedades Trop* Mexico 1944 Mar v 5 No 1 31-6 English summary

The healthy persons tested were 603 women, 61 school children and 336 elderly people of both sexes in a charitable institution. The antigen used was prepared by the technique of BOZICEVICH [this *Bulletin* 1939 v 36 847]. It produced in susceptible individuals reactions similar to those produced by antigen received from the National Institute of Health. The authors injected 0.01 cc. the reaction being read 30 minutes later. The dilution used is not stated. A papule of 3 mm. or more in diameter with or without pseudopodia was regarded as positive, this being the authors' say the criterion recommended by Bozicevich (*loc cit*) when 0.01 cc. of a 1:10 000 dilution is used. By this criterion their percentage of positives was 17.9. Using the criteria recommended by McNAUGHT BEARD & MAYERS [this *Bulletin* 1942, v 39 194] in which a papule of 4 mm. in diameter obtained by the injection of 0.01 cc. of antigen is regarded as approximately equivalent to one of 7 mm. in diameter obtained with 0.1 cc. of antigen at a dilution of 1:10 000 the authors' percentage of positives was 13.8. Using the instructions issued with Lilly's antigen and taking a papule of 8 mm. diameter obtained with 0.01 cc. of antigen as approximately equivalent to one of 15 mm. obtained with 0.1 cc. of antigen the authors' percentage of positives was only 2.2. The results confirm the authors' view of some workers that more precise data are required before this test can be correctly evaluated.

G Lapage

TAYLOR, E. L. A Search for Endemic Areas of Trichinosis in Great Britain. [Correspondence.] *Nature* 1944 June 17 745-6

This paper is reviewed in *Bulletin of Hygiene* 1944 v 19 767

DEFICIENCY DISEASES

PAULLEY J W & AITKEN G J. Case of Cardiovascular Beri-Beri. *Lancet* 1944 Sept. 30 440-42.

Another well recorded case showing that the term beriberi¹ covers more varied conditions than the classical dry and wet types described in the text books. Seven years ago WEISS & WILKINS called the attention of the medical

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world to cardiovascular disturbances in patients with peripheral neuritis ascribed to alcohol excess they noted the frequency of this in the United States and they expressed the view that some such cases at least were fundamentally beriberi. Since certain of the signs characteristic of text-book beriberi are absent Weiss and Wilkins suggested that the name at first given to the syndrome beriberi heart should be replaced by "cardio-vascular beriberi," because the heart failure was largely brought about by changes in the peripheral circulation, in combination with diet deficiencies.

The subject whose case is here recorded was a man of 45 who had been in the Air Force in Persia and Malta for 2½ years and in Cyrenaica for 7½ months. He noticed, apparently suddenly an aching of the calves with shortness of breath and rapidity of his heart's action. He was an athletic man for his age. His legs became swollen and soon afterwards his arms also this swelling was worse at the end of the day subsiding to some extent during the night. A medical officer put him through an exercise-tolerance test and the pulse had not returned to normal in 1½ minutes. After a week in bed the oedema subsided, but any exertion brought on dyspnoea and palpitation. The calves were tender even the pressure of the bed-clothes causing discomfort. The calves and regular the pulmonary second sound was accentuated the liver and spleen could be felt two fingers-breadths below the costal margin. The character of the reflexes were present the knee-jerks exaggerated supinators sluggish as was also the right ankle-jerk there was no impairment of sensation to cotton wool or pin prick but the calves were very tender. Inquiry into the diet revealed that he had had half rations at Malta and desert diet for more than two years for a month and a half he had had no fresh food. His alcohol consumption was 5-6 tots a day including Cyprus brandy sherry liqueur, local gin or whisky. The arm-tongue circulation time was just above the upper limit (16 sec.) no electro-cardiographic abnormality. Vitamin B₁ excretion in place of 4-5% the normal minimum (1-6 units in place of 18-56) and was less than one-tenth the normal. The arm-tongue circulation time was only 11 L.U., after a subcutaneous test dose of 5 mgm thiamin the output was only 11 L.U., or about one-twentieth of the normal.

The patient was made to rest and was given a diet high in protein and calories with thiamin 10 gm daily at first subcutaneously later orally. After 40 days there was no oedema, no aching of calf muscles no dyspnoea or palpitation on exertion the arm-tongue circulation time was 7 sec the blood pressure 142/94 exercise tolerance 78-108-78—in short he left hospital recovered.

H. Harold Scott

ROBERTS D W & NAJJAR V A A Case of Pellagra developing on a Hospital Ward in a Patient receiving Vitamin B Complex. *Bull Johns. Hopkins Hosp* 1944 June v 74 No. 6 400-405 4 coloured figs

The case here reported is that of a 12 year-old girl (white) admitted to the Harriet Lane Home Baltimore on account of anorexia, fatigue and loss of weight of more than a year's duration who after eight weeks under care in hospital on the hospital diet supplemented with yeast developed signs which led to a diagnosis of pellagra. These consisted of pigmentation of the backs of the fingers, limited above by the line of the knuckles, and about the elbows together with a red tongue which cleared up rapidly after the administration of 100 mgm nicotinamide four times a day by mouth. The skin cleared up very much more slowly.

The diagnosis of pellagra was confirmed by failure to detect fluorescent factor F2 (N methyl nicotinamide derivative) in the urine even after a test dose of 100 mgrm. nicotinamide by mouth. The past history as first obtained was unimportant and detailed investigations were negative but subsequently it was revealed that the child had suffered for 18 months and was still suffering from diarrhoea (the child had been allowed access to the lavatory). The cause of the diarrhoea was not ascertained after extensive examination and it did not respond to nicotinic acid, sulphasuxidine and sulphaguanidine. The preparation of yeast was found to contain very little nicotinic acid. There ensued an attack of cardiac failure to which the child nearly succumbed treated with digitalis intramuscular liver extract and intravenous vitamin B concentrate. From this time improvement took place and the diarrhoea gradually ceased.

The authors conclude that as the result of some obscure intestinal disorder (possibly a regional ileitis) there was interference with the absorption of nicotinic acid by the bowel.

H S Stannius

GHALJOUNGUI P. Secondary Pellagra. [Correspondence] *Lancet* 1944 Sept 23 422-3

The author refers to an annotation in the *Lancet* of June 3rd 1944 entitled Secondary Pellagra which deals chiefly with a paper [on pellagra in the U.S.A.] by BEAN SMIES & BLANKENHORN (*Medicine* 1944 v 23 1) and which expresses the view that the main factor involved in the production of so-called secondary pellagra is malnutrition among large sections of the inhabitants such as is unknown in Britain.

In this letter Ghaljoungui writes of pellagra in Egypt and states that it occurs there after severe protracted diarrhoea and in prisoners on heavy manual work who often have intestinal disease as well. The only important group consists of cases of endemic pellagra as seen in the fellaheen. He gives reasons for the view that pellagra is closely related to helminthic infection especially schistosomiasis and ankylostomiasis. The diet of the fellaheen is probably only just sufficient so any disturbance of absorption or any excessive demand by hard work will upset the balance. All pellagra in Egypt might be considered secondary but the author sees no point in distinguishing between primary and secondary pellagra.

J F Corson

FISHER G E. The Esophageal Manifestations of Pellagra. *Southern Med J* 1944 Aug v 37 No 8 446-8

The author states he has been unable to find any description of the mucosal lesions in the esophagus of persons suffering from pellagra. Oesophagoscopy was carried out on 17 pellagrins complaining of dysphagia 24 to 72 years old of whom 12 could not take any solid food. The mucous membrane was intensely hyperaemic and in some cases oedematous with multiple tiny ulcers present in nine. Barium studies in eight showed small constricted areas corresponding to those in which ulceration was present. All the patients had glossitis. Several are mentioned as presenting haemangioma like lesions of the conjunctiva.

After treatment with nicotinic acid, riboflavin and thiamin had been instituted the dysphagia was relieved in from three to eight weeks. Only one case is stated to have been re-examined in that case the mucous membrane was normal.

H S Stannius

MCCREARY, J. F. & TISDALL, F. F. Further Studies on the Relationship of Corneal Vascularization to Riboflavin Deficiency. *Canadian Med. Ass. J.* 1944 Aug. v 51 No 2, 103-10 2 figs.

Reference should be made to a previous paper [this *Bulletin* 1944 v 41 63]. In this summary the authors state (1) The results obtained from photographing the corneoscleral junction and by an examination with a slit lamp are not significantly different. Elsewhere, however they say vessels which do not contain blood are more difficult to see in photographs than with slit lamp examination. With black-and-white photographs the corneoscleral transition zone is almost indiscernible from the cornea proper thus making assessment of the extent of invasion in relation to this zone difficult. In the photograph it is difficult to distinguish between vascularization in this zone and that of the cornea proper. [The only advantage of the photographic method would therefore appear to be that it provides a permanent record of blood-containing vessels. It can in no way replace slit lamp microscopy.]

"(2) A study to demonstrate the effect of riboflavin on corneal vascularization has been carried out. The subjects of the investigation consisted of (a) 16 persons who had lived for a year past on a diet which when served contained 2.9 mgm. of riboflavin per diem these were the controls their diet remaining unchanged during the inquiry. (b) 25 persons on the same diet to which a supplement of 3.3 mgm. of riboflavin thrice daily was added for two months. Under the conditions of this study there was no consistent change in corneal vascularization in either the treated subjects or the controls."

No correlation could be established between any changes in corneal vascularization and any change in symptoms.

The authors conclude "So far as this study shows, it seems that a uniform peripheral corneal vascularization is not a safe basis for a diagnosis of riboflavin deficiency. [It is important, however to observe the method of notation adopted in this study. Cases were divided into groups according to four stages—0 no vessels beyond the sclera. 1 vessels present in transitional zone by which the authors appear to mean the limbus. 2 some vascular twigs passing into the clear cornea. 3 vascular loops in clear cornea. Their cases are—

	Stage 0	Stage 1	Stage 2	Stage 3
16 controls	1	4	10	1
25 supplements	1	15	8	0

In the experience of the reviewer stage 1 is not a stage in vascularization but within the normal, stage 2 may contain many cases which should be considered as within limits of normal. This leaves only a single case out of the total 41 which may have resembled the condition commonly ascribed to riboflavin deficiency.]

H. S. SLAVINS.

HAEMATOLOGY

MURPHY, R. C. Jr & SHAFIRO, S. Sickle Cell Disease. I. Observations on Behavior of Erythrocytes in Sickle Cell Disease. *Arch Intern Med.* 1944 July v 74 No 1 28-35 [25 refs.]

It would appear that this is merely the first of a series of papers on this interesting but obscure condition—interesting because of the recognition of its

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increasing prevalence obscure because of the many as yet unsolved problems connected with it. Sicklaemia seems to be much more common than is usually believed. It is estimated that at least 7 per cent of all American negroes show it. Though the sickling may be affected by environmental factors it is a property inherent in the erythrocytes and not dependent on the other elements of the blood.

The source of blood for the authors studies was a male Negro 21 years old with severe sickle-cell disease. The authors instead of placing a coverslip on a drop of blood and sealing the edge apply a coverslip on which a thin film of petrolatum has been spread to a drop of blood and press it down thus an even suspension is formed free of air bubbles. Sickling begins with a concentration of haemoglobin at the periphery (doughnut appearance) then a thinning occurs at some point and the cell ruptures to form a crescent. As soon as sickling occurs the corpuscle which was mobile becomes fixed rigid and brittle. This assumption of abnormal shape takes place whether the cells are in homologous serum foreign serum or saline but is more marked in whole fresh blood than in serum or saline solution. It is therefore a characteristic inherent in the susceptible erythrocyte itself. When exposed to air as by raising the coverslip the sickle cells return at once to the normal shape. [This is strange seeing that the corpuscles are said to have ruptured]. In other words corpuscles with oxygenated haemoglobin do not sickle they do so only when the haemoglobin is reduced. Again the pH has per se no effect as regards sickling. Further studies convinced the authors that variations in ionic balance play no part in the sickling nor probably is it due to complex metabolic change for it is rarely seen in reticulocytes normoblasts and young forms. Further investigations may show to what extent oxygen tension or degree of dissociation of haemoglobin—variations in the sickling threshold—may explain crises in the disease of sicklaemia. In their summary the authors state: Sickling is a property inherent in the susceptible erythrocyte. It appears to be encouraged by coagulation of the blood specimen. Erythrocytes sickle at various specific thresholds as determined by the ratio of dissociated to combined haemoglobin. There is evidence to indicate that as the cells age the sickling threshold becomes lower. H Harold Scott

MALHOTRA R. P. & CHUTTANI P. N. A Case of Cooley's Anaemia. *Indian Med Gaz* 1944 May v 79 No 5 198-9 1 chart

COOLEY in 1927 first described a remarkable anaemia associated with splenomegaly and bone changes occurring almost exclusively in children of Mediterranean origin. Since then cases have been described almost all over the world and with rare exceptions it has been possible to trace some admixture of blood from Mediterranean stock. However four cases have recently been seen in India and another has now been added to the list by the present author. The child aged four years was of pure Punjabi stock. He had anaemia of the characteristic type the red cells showing great anisocytosis and many primitive forms splenomegaly and the typical changes seen in the bones of the skull. Unfortunately no mention is made of possible malarial infection. Janet Vaughan

SUNDARAM S. K. Refined Liver Extracts in the Treatment of Nutritional Macrocytic Anaemias. *Indian Med Gaz* 1944 June v 79 No 6 253-6 [12 refs.]

There has been considerable conflict of opinion in the past as to whether highly purified liver extracts like anahaemin are effective in nutritional macrocytic anaemia. Sundaram has described the treatment of 15 cases of nutritional

macrocytic anaemia with and without diarrhoea which, with two exceptions responded well to refined liver extract of the anahaemin type. In one of the failures there was subsequently no improvement when crude extracts were given or after blood transfusion. In both, septic and infective inhibiting factors were present. In some cases there was a satisfactory reticulocyte response, in others in spite of severe anaemia there was a rise in red cells and haemoglobin to normal levels with only small increase in reticulocytes. He suggests that possibly too much emphasis has been laid in the past upon the reticulocyte response as a measure of the effectiveness of an extract, and that before discarding an extract as useless there should be a delay of six to eight weeks during which a constant watch is kept on the whole blood picture. Since the patients studied showed no improvement during a control period on a good hospital diet alone without liver therapy, Sundaram concludes that the diet cannot be responsible as has been suggested for the improved condition. The total dose was approximately 12 cc given intramuscularly in injections of 2 cc. on alternate days. The improvement in the blood picture was associated with a similar improvement in the glossitis and diarrhoea, whether fatty or not. One patient seen in a subsequent relapse responded equally well to large doses of marmite. The author admits that the action of crude extracts is more rapid than that of the purified extracts but prefers the latter because of what he calls its depot action.

Jand Vaughan

LOWE A & NIELSEN H E Paroxysmal Paralytic Hemoglobinuria. *Acta Med Scandinavica* 1944 v 117 No. 5/6 424-36 3 figs. [10 refs.]

Though describing a rare disease this article is of the highest interest and calls for full abstract. According to the authors their case is only the fifth to be recorded in medical literature. As a preliminary, they give the following classification of haemoglobinurias —

- A Exogenous.
- 1 Infectious Typhoid fever malaria, scarlet fever sepsis.
 - 2 Poisoning Chlorates, phenols, pyrogallol, quinine, sulphonamides (they omit snake-venom).
 - 3 After blood transfusion.
 - 4 Half disease (see *Bulletin of Hygiene* 1942, v 17 197 where other references are given).
 - 5 Ferism (see below p. 61 where other references are given).
- B Endogenous
- 1 Cold haemoglobinuria (patient usually asplenic).
 - 2 March haemoglobinuria.
 - 3 Chronic haemolytic anaemia (myoglobinuria) [a better name]
 - 4 Paralytic haemoglobinuria (myoglobinuria)

It is the last which is the main subject of the author's paper. They give brief records of the four previous cases [STIRR in *Tropical Diseases* merely says that it has been reported in a few human cases.] (i) A boy of 13 years, who had had a similar attack four years before, reported by Meyer Bits in 1911. (ii) A woman of 42, reported by Paul of Vienna in 1924. (iii) A man of 54 reported by Günther of Leipzig the same year. (iv) An adult woman, reported by Hittmair of Vienna in 1925.

The details of the authors case are as follows. A boy of 10 years was admitted to hospital as a suspected case of progressive muscular dystrophy. The family history of this was quite typical in the five generations inquired into. The first, a man with this disease, had emigrated from Sweden to Jutland he had two daughters free from the disease. One of these had four sons and four daughters and three of the sons were victims. The other daughter had four

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sons and six daughters and two of her four sons were attacked that is five of eight males but none of the ten females of the third generation. In the next two more males suffered and the patient who is the subject of this article belonged to the fifth generation. This boy was in excellent health till the age of four years since then he had had repeated attacks of pain in the [leg] muscles and transient difficulty in walking during which the calves were firm and tender and he passed bloody urine. There was slight enlargement of the calf muscles. He left hospital nine days later (there being no symptoms in the interval) with the provisional diagnosis? Incipient progressive muscular hypertrophy. Three weeks later he was again brought to hospital with a history of a sudden onset of intense pain in the legs when he was on the way to school. He had great difficulty in walking and his gait was laborious and waddling and obviously painful. He passed dark reddish brown urine giving the reactions for albumin and blood, but no corpuscles were seen. Blood examination gave red cells 4.3 millions beginning to haemolyse at 0.44 per cent NaCl haemolysis complete at 0.35 per cent white cells 6,200 Hb 100 per cent platelets 51 monocytes 6 per cent. The leucocyte differential count was neutrophils 43 lymphocytes 51. Spectroscopic examination showed that the urinary convulsion was due to myoglobin and during the attack there was considerable creatinuria which disappeared as the urine cleared.

Comparison of the main features of paralytic myohaemoglobinuria and the hypertrophic form of progressive muscular atrophy shows that they possess several characters in common. The same muscles are attacked, creatinuria is present, periodic in the former permanent in the latter. If death occurs and two of the four previously recorded did die—the muscles were seen to be pale (fish muscles) and atrophic with striation indistinct, the fibres degenerated and fragmented with increase in the number of nuclei. Progressive muscular dystrophy and paralytic myoglobinuria may be different forms of the same disease, the latter representing the acute manifestation of the lesion while progressive muscular dystrophy is the more chronic form of the disease.

In future when cases of progressive muscular dystrophy are met with it would be of interest to inquire into the family history bearing the foregoing facts in mind.

H Harold Scott

JOSEPHS H W Favism. Bull Johns Hopkins Hosp 1944 May v 74
No 5 295-8 1 fig.

The case is recorded of a boy of five years of Greek parentage who while in apparently perfect health was attacked by abdominal pain accompanied by rise of temperature jaundice and the passage of dark urine. He gave a history of a similar attack, lasting for ten days eleven months previously. In the present attack there had been repeated mild epistaxis four days before the patient's admission to hospital. At the time of admission there was marked pallor with jaundice but no albuminuria. Blood examination gave red cells 1,900,000 white 28,700 per cmm. with occasional erythroblasts haemoglobin 4.5 gm. The only ascertainable cause was a meal of fava beans eaten two days prior to the onset of symptoms. One month after his admission when recovery was practically complete (red cells four million per cmm haemoglobin 13.5 gm.) he was given eight fava beans soaked in water and four days later symptoms indicative of favism appeared. Skin tests with extracts of the bean were negative but this is often—one might say usually—the case for some time after an acute attack. Seeing however that the skin reaction is given in certain circumstances favism is probably to be placed among the allergic diseases. Racially the Mediterranean race is mostly susceptible (cf Cooley's anaemia).

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and the disease is common in Sardinia. The present patient was a Greek and the patient whose case was recorded by EADS & KASH (this Bulletin 1944 v 41 238) was of Spanish stock. [The author has made two small slips. First in stating that only twice has it been reported in this country "i.e. the United States of America" secondly that the fava bean is "not grown in this country. The two instances he refers to were reported by McCART & ULLENT (J Amer Med Ass. 1833 v 101 1399) and by J E. HORTON (ibid., 1837 v 109 1818). In addition there is the one by EADS & KASH referred to above reported in the U.S. Nav. Med. Bull. in November 1943. Secondly though *Vicia faba* beans are usually imported, the plant is now according to Eads and Kash, being cultivated in the United States. Hence it is not improbable that cases will be more frequently met with]

H. Harold Scott

VENOMS AND ANTIVENENES

COCHRAN Doris M. *Poisonous Reptiles of the World* a Wartime Handbook. Smithsonian Institution War Background Studies No. 10 (Publication 3727) Wash. 1943 Mar 19 37 pp. 17 pls. (1 coloured) & 2 figs. [15 refs.]

This beautifully illustrated handbook gives a brief outline of the distribution, anatomical features and habits of most of the poisonous snakes and lizards of the world. The text is interesting and instructive in a general way but is not apparently intended for a field worker. A simple discussion of the differentiation between poisonous and non-poisonous reptiles, and possibly some elementary keys to identification would have greatly improved the book.

The descriptions of snakes are clear but not always accurate. For example the statement that spitting cobras "blow their venom into the face of attacker is incorrect. The ejection of venom is brought about primarily by muscular action and the accompanying expulsion of air is of secondary importance. Further there is no evidence that the snake aims its venom at the eyes. The direction of the venom stream is determined by the attitude of the snake when spitting. The direction and the aim can therefore be only in the general direction of the victim. The description of the effects of ejected venom on the intact eye is highly coloured. The common effect of such venom is a painful, rapidly developing conjunctivitis, readily amenable to simple mechanical treatment by washing with saline or warm water.

The statement on page 18 that muscurana is unaffected by the injury of the fangs is loosely worded. The same applies to the description of the physiological activity of viperine poison, which is stated to "dissolve the endothelium cells composing the wall of blood and lymph vessels."

In the section on the African snakes *Naja melanoleuca* should have been described as a black-and-white cobra since the common specimen has its dorsal black scales fringed or tipped with brilliant white and is usually spotted with white in the labial and neck regions. The same applies to *Naja nigricollis* is a little misleading. The commonest variety is black dorsally with steel grey belly liberally blotched and banded in the neck and throat with salmon pink (not simply with a pair of large crimson blotches under the hood). There are some curious omissions. For instance, the genera *Atheris* and *Atractaspis* are not referred to amongst African snakes, although the latter genus is one of the commonest poisonous snakes in the British West Coast Colonies.

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The advice of the Appendix regarding the treatment of snake bite is dangerous. So many snakes particularly the African cobras dribble and spray their poison over the surface of the area bitten that all notes on first aid in snake bite should convey the warning that additional cuts in the region of the bite must never be made until the area concerned has been well washed (with urine or spulum if no water is available) to remove venom from the surface. Cutting in the region of an unwashed bite amounts to a possible further introduction of venom into the tissues. In dealing with snake bites the dogmatic assertion on page 25 that in viper poisoning the administration of alcoholic drink even in small quantities is absolutely fatal is based on very slender evidence and is certainly not the experience of the reviewer. Such comments are out of place in a booklet of this sort.

The general impression gathered in reading this little book is that it is a well illustrated museum guide written around exhibition specimens.

B G Macgrath

[AUSTRALIAN MILITARY FORCES.] The Dangerous Snakes of the South-West Pacific Area. 43 pp 11 figs & 3 pls. Notified in G.O.s dated 1943
By Authority Victorian Railways Printing Works North Melbourne — 3480/43

This is a very useful little handbook well arranged and clearly written designed for the intelligent layman and including sufficient detail on most of the poisonous snakes of the Area. The text is divided into sections for convenience for identifying specimens and it contains useful drawings of the principal genera. There is an interesting introduction which outlines the geographical distribution of snakes and of the differentiation of venomous and non venomous types. There is also a key to the dangerous snakes of the Malay Islands, Celebes and Philippines of North Australia New Britain New Guinea and Ceram and of the Solomon Islands.

The pamphlet also includes a good practical summary of snake bite and its first-aid treatment. It should be of real value to Medical Officers and to other Officers and N.C.O.s in charge of troops.

As is almost inevitable in a small work there is some unbalance in the description of the genera distinguishing features of several species being given in some genera but not in others. There is also a change in notation in the heading of the section devoted to the tiger snake which may be confusing to the reader thus under this title both generic and specific names are given whereas only generic names are given for other snakes. The heading Pit Vipers and the accompanying paragraph on page 19 would be better placed on page 20 where pit vipers are described. The generic name for humped nose pit vipers is given with the American spelling and although this is widely accepted the classical spelling *Ancistrodon* is preferable.

More stress could have been laid on eye size and pupil shape in the other wise clear diagrams. It is not possible to distinguish between the vertically ovoid pupils of the Russell's viper and the round pupils of the cobra.

Some of the information on points of detail is misleading. For instance it is stated that in *Trimeresurus* the body scales have longitudinal keels thereby producing a file-like surface to the back. Since such keeling is common to other genera described in the book it is a pity that emphasis should have been laid on it in this genus in so many of the species of which keeling may be almost completely absent and the scales may be practically smooth. Keeling of scales is also described as a characteristic of *Oxyuranus* although in KINGHORN'S original description the scales are described as smooth the comment being

added "a few of the central rows of the dorsal scales appear to bear obtuse keels but tells me that he is almost certain the scales were smooth in the living snake."

Some of the anatomical descriptions of other snakes are not quite accurate which is unfortunate since, in most cases, such information as is given is not essential for the rough identification of genera for which the pamphlet was prepared (see for example, the description of the subcaudal scales in kraits and the cobras etc.)

In the description of the *Demansia* genus the statement that the anal shield is paired is not strictly correct since in *D. ornaticeps* (Port Darwin) the anal shield is entire. B G Macgregor.

MACGREGOR B G The Identification of the Poisonous Snakes of British West Africa. II.—Details of Genera and Species. *Ann. Trop. Med. & Parasit.* 1944 Sept. 30 v 38 No 2 119-33.

Part I of this excellent work has been referred to in this Bulletin [1944 v 41 604]. This second part gives details of 37 species of Colubridae belonging to three genera of Elapinae, six genera of Viperinae of the Proteroglypha, and 14 genera of Dipsadomorphinae (Opisthoglypha). Under each genus is given briefly the species, the common names and notes covering the salient characters of all and their venom. Each species is considered and described systematically—the head, the teeth, the eyes, the head-shields and the body scales. When the whole work is completed permission should be obtained to have it issued as a separate publication so that all those interested in or concerned with the identification of snakes of West Africa may have it at hand and not have to turn up bound volumes of the *Annals* for the information required. H Harold Scott.

PURDHIE G R *Eckis carinata* Poisoning. *Indian Med. Gaz.* 1944 June v 79 No. 6 206-8.

The venom of *Eckis carinata* contains an ant clotting ferment, an haemolysin and a potent haemorrhagin hence the effects of a bite by this snake are haemorrhages which may occur anywhere—from the gums as subcutaneous extravasations, from the urinary or intestinal tract, etc. Locally there is severe burning pain, swelling and bleeding from the punctures for a long time, and later sloughing of tissues. Local treatment is not, as a rule, very effectual, for the patient usually applies it after several hours and in many cases has assisted absorption by running a distance to obtain aid. Specific treatment by intravenous injection of 10 cc. of concentrated antivenene should be given as early as possible (but the author does not seem to place much confidence in this). Beneficial treatment is mainly symptomatic comprising cardiac stimulants, vasoconstrictors (adrenaline pituitrin) and calcium to hasten coagulation and repair of the vessel wall. The author finding it difficult to procure haemostatics locally tried intramuscular injection of 2-3 cc. human serum and reports two cases in which the oozing of blood which had persisted for three to four days, ceased within 24 hours of injection of the serum. (In a third case, apparently more severe than the other two the bleeding from gums, urethra and bowel ceased spontaneously after three days a fact which detracts somewhat from the value of the two reported cases as to the efficacy of the serum. Further trial is needed.) H Harold Scott.

EARLE K V Snake Bites in Northern Peru. *J. Trop. Med. & Hyg.* 1944 Aug-Sept. v 47 No 4 37-40 3 charts

Reptiles are common in Northern Peru in the desert area of Talara Negritos nevertheless cases of snake-bite are few. During 1943 the author who is

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Medical Director of the International Petroleum Company and was formerly Chief Medical Officer of the Negritos Hospital Peru saw only three cases all bites by the *machancho* or *Trimacrus barnelli* a variety of *ser-de-lan* etc. The symptoms in the three cases described do not seem to have been very severe they comprised a certain degree of shock local pain and oedema extending for some distance up the limb some albuminuria (not great) and in one patient, haemorrhage from the oral mucosa about 15 hours after the bite.

Antivenene was injected intravenously in one intramuscularly in two (one of these had received the intravenous dose) in the third the route of administration is not mentioned. Recovery in each case was rapid two left the hospital in three days the third was much better in three days and left hospital on the sixth day.

Another poisonous snake in Peru is the coral snake' *Micrurus tschudi* others e.g. *Constrictor constrictor orlonis* are of the *Boidae* and are not poisonous though dreaded by the inhabitants. H Harold Scott

SAMPAYO R R L. Pharmacological Action of the Venom of *Latrodectus mactans* and other *Latrodectus* Spiders. J Pharm & Exper Therap 1914 Apr v 80 No 4 300-322 7 figs. [13 refs.]

An interesting study on the mode of action of the venom of *Latrodectus mactans* the Black Widow spider. Poisoning by the bite of one or other of the eight known species of *Latrodectus* is frequently met with in North and South America in Italy Spain and Russia in South Africa and Madagascar. Before detailing his studies of the venom the author describes the symptoms caused by the bite. These are familiar to readers of this *Bulletin* (see especially 1936 v 33 401). He then refers to an antivenene prepared from horses by injection of triturated cephalothoraces in saline and its beneficial results when injected subcutaneously in a dose of 10 cc.

The action of the venom is then considered and from his work the author has noted (1) *The action on the Motor System*—Initial tremor then muscular contractions and stiffness of the muscles of the abdominal wall (in guinea-pigs and dogs) but not in denervated muscles. The action is not direct but via the central nervous system. (2) *On the Vascular System*.—Intravenously injected the venom raises arterial pressure by generalized vasoconstriction. It has no effect on adrenaline secretion. There is always a latent period between injection of the venom and the onset of symptoms, as though there was a slow central nervous penetration or some chemical transformation. The hypertension produced is probably of central origin but a fresh venom though highly toxic may have little hypertensive power. Rise of blood pressure occurs after injection of the venom even in decapitated animals and after extirpation of the carotid sinus and section of both vagi indicative of direct action on the spinal cord. The hypertension is not prevented by atropine it is reinforced by cocaine. The venom has no effect on involuntary muscle bronchioles intestine, uterus but by thoracic and abdominal muscular spasm causes irregular breathing and periods of apnoea. H Harold Scott

GHOSH, T K. Cobra Venom Therapy of Pain of Malignant Disease with special reference to Carcinoma of the Cervix. *Calcutta Med. J.* 1944 June, v 41 No 6 185-90

DERMATOLOGY AND FUNGOUS DISEASES.

FLECKER, H. & MCSWEENEY A. Irritation produced by the Procession Caterpillar (*Ochrogaster contraria*) *Med J Australia* 1944 Aug 5 v 2 No. 6 137-8.

The procession caterpillar—so called because they follow one another in numbers across tracks at night—the larva of a moth *Ochrogaster contraria* forms nests in bags of filty and more in trees. If these nests fall and the caterpillars alight on anyone beneath, the hairs set up an irritative dermatitis—a diffuse erythema with intense itching or a patchy urticaria—wherever the come in contact with the skin. Three cases are recorded, in soldiers occupy a tent beneath a tree in which such a nest was present. Fomentations with 1 per cent. Dettol, followed by calamine lotion in half an hour brought speed relief. If the urticaria was severe 10 minims of 1:1000 adrenaline were injected subcutaneously twice a day for two days. [See also this *Bulletin* 1927 v 400] H Harold Scot

MENDELSOHN H. V. Dermatitis from Lemon Grass Oil (*Cymbopogon citratus* or *Andropogon citratus*) *Arch Dermat & Syph.* 1944 July v 50 No 1 34-5.

Among the many known causes of dermatitis venenata mentioned in standard works—those of J. C. WHITE, L. F. WEBER, V. PARDO-CASTELLO and R. PROSSER WHITE, for instance—lemon grass oil, the oil distilled from *Cymbopogon citratus* receives no mention. It has an odour like that of verbena contains 70 per cent or more of aldehydes, the chief of which is citral, and is used for making perfumes. The plant is indigenous to East India.

The author had under his observation eight men who suffered from erythematous, squamous and vesicular dermatitis after working on a boat which had recently come from India with a cargo of lemon grass oil. It affected the face, forearms, ankles and eyelids. A sample of the oil itself was not obtainable but reactions resulted from the application of pinewood contaminated with the oil. It seems to be not only a direct irritant but also to act as a sensitizer for an incubator period of 6 to 18 days may elapse before symptoms arise. It may be noted that the oil—widely used as an insect repellent—is obtained from another species of *Cymbopogon* namely *C. nardus*. H Harold Scott.

EVERAID, H. Triple Symptom Complex of Babes. Report of a Case. *Arch. Dermat. & Syph.* 1944 July v 50 No. 1 37-8.

MICHAEL, P. McLAUGHLIN R. F. & CRYNAC, P. L. Coccidioidomycosis. Report of Unsuccessful Treatment with Penicillin. *U.S. Nav Med Bull.* 1944 July v 43 No. 1 122-4

Although previous experiments *in vitro* and isolated tests of the therapeutic use of penicillin in the treatment of coccidioidomycosis gave no evidence of its effectiveness in the treatment of this disease the authors decided to try the effect of unusually large doses of the drug on a case under their care. The disease was, apparently of some duration and the clinical features pointed mainly to internal hydrocephalus but the diagnosis of coccidioidomycosis was made only after the appearance of two superficial abscesses on the chest wall, from which *Coccidioides immitis* was isolated. The fungus was, later also cultivated from the cerebrospinal fluid. After the diagnosis, penicillin treatment was administered and a total amount of 3 081 000 Florey units was given 500 000 units intrathecally and the remainder intravenously.

drug had no noticed effect on the course of the disease and death occurred four months after symptoms had first been observed. A post mortem examination revealed extensive generalized disease affecting most of the organs. The base of the brain was covered by a tenacious fibrinopurulent exudate and there was marked internal hydrocephalus with dilatation of the ventricles and oedema of the choroid plexus

J T Duncan

MONTPELLIER J & CATANEI A. Nouveau cas de dermatite verruqueuse mycosique observé en Algérie. [A New Case of Cutaneous Mycosis seen in Algeria.] *Arch Inst Pasteur d'Algérie* 1944 Mar v 22 No 1 13-15

The authors give a brief account of their examination of a piece of morbid tissue removed at biopsy from a case of chromohlastomycosis which occurred at Constantine in Algeria. The causative fungus was isolated in culture and identified as *Phialophora verrucosa*. An earlier Algerian case of this disease reported by the same authors in 1926 was caused by *Hormodendron algeriense* n. sp

J T Duncan

SAVER, A. Blastomycosis of the Skin (Glehrst Type) with associated Blastomycetell Pulmonary Disease. Report of a Case. *U.S. Nav. Med. Bull.* 1944 Aug v 43 No. 2, 333-42, 5 figs. (10 refs.)

MISCELLANEOUS DISEASES

FERRO-LUZZI G. Altitudine e malattie dell'apparato circolatorio (Ricerche cliniche e sperimentali.) [Altitude and Heart Disease. Clinical and Experimental Research.] *Boll. Soc. Ital. di Med. e Igiene Trop.* (Sez. Entren) 1944 v 3 No 1 9-88 7 figs. on 6 pls. English summary 87-8.

The author studied during 5 years the clinical aspects, the course and the prognosis of the diseases of the cardiovascular system. The investigation was performed on 871 Europeans living in the Entrean highland (2 400 m.). The first part of the work deals with the phenomena induced by altitude on the circulatory system in healthy subjects. Such phenomena are demonstrated to be of two kinds: mechanical and metabolic. The first produces a decrease of blood volume accompanied by a corresponding contraction in diameter of peripheral vessels without increase of heart activity. The second causes an increase in the metabolic rate of the tissues and a condition of compensated gaseous alkalosis with a decrease in alkali reserve.

As the author points out, the above mentioned phenomena act harmfully and simultaneously on the oxygen balance in the tissues, altering the nutritional quotient between supply and demand and thus giving rise to a chronic malnutrition of the tissues which sometimes becomes evident in the myocardium as well.

In the second part of the paper the author examines the principal diseases of the cardiovascular system with special reference to the influence of them on altitude. The following diseases have been studied: chronic valvular diseases, apparent primary myocarditis, secondary myocarditis, hypertension, aortitis, anginal syndrome, disturbances of heart rhythm, circulatory baropathies, sepsis with carditis. In all these diseases the author has investigated particularly the myocardial damage both clinically and by means of electrocardiography, telerradiography and arterial and venous pressures. The results obtained in these investigations revealed that though the altitude

does not bring about, in the above mentioned diseases, a more frequent or more severe myocardial damage than in Europe the damage shows, more frequently than elsewhere, an evident coronary type—a phenomenon which constitutes according to the author the most striking feature of cardiopathies evolving in altitude.

The author also calls attention to a syndrome observed by him in the Eritrean highlands and which he presents and describes proposing to describe it with the term circulatory baropathy. This is represented by a functional disease of the circulatory system, which the author assumes to have for its basis an insufficient adaptation to the biological conditions imposed by altitude.

The third part of the work deals with the principal metabolic changes induced by altitude in patients with cardiopathies (basal metabolism, acid-base balance haemochemical values and so on). As to basal metabolism, a considerable increase is noted. With regard to the acid-basic balance, a condition almost constantly a situation of compensated non gaseous acidosis which leads to a further decrease of alkali reserve. The author discusses of blood have been generally found within normal limits. The author discusses as well the value of vitamins A, B, C in relation to cardiopathies.

Concerning heart failure the author calls attention to 2 principal facts
(1) heart failure does not occur very frequently in highlands.
(2) Once the heart failure develops it is always more severe than in Europe.

The author suggests that there is good reason to assume that both these observations represent a sequence to the damage induced by altitude on the peripheral vascular system. This peripheral damage is perpetuated by the interference of metabolic changes and it deprives the circulatory system of one of its principal functional reserves. A further reason of such abnormal behaviour of heart failure has to be investigated in the coronary feature of the myocardial damage. Furthermore the author discusses the practical value of statistical data of mortality from cardiopathies in Europeans living in Entrea, and examines the prognosis of heart disease in this country. He points out that, whilst the mortality from heart failure is not high that from anginal syndromes is remarkable. The author thinks that such peculiar behaviour is a consequence of the peripheral circulatory system's reaction to altitude.

Finally in the last part of the work the author discusses the treatment of heart diseases, with or without heart failure, in the highlands. Experiments as to the favourable influence of thyroidectomy in heart disease at this altitude, have been carried out, but the number of patients so treated is not sufficiently large at present to permit a report.

FLECKER H. Sudden Blindness after Eating = Finger Cherries (*Rhodomyrtos macrocarpa*) *Med J Australia*. 1944 Aug 19 v 2 No 8 183-5 1 fig

This is a most interesting contribution. Brief records are given of children suddenly becoming blind some 24 hours after eating finger cherries, the fruit of *Rhodomyrtos macrocarpa* a plant growing in North Queensland. Some of the cases recorded are of patients attacked 33 to 51 years before and none later than 14 years ago so the histories may not be accurate in detail, but the general history was of eating the fruit in some instances unripe, in others overripe, and suddenly 24 hours or a little less afterwards becoming blind and in nearly all cases remaining permanently so. Ophthalmoscopically optic atrophy was found. [No other symptoms are mentioned and it is certainly strange for a poison to have so limited and specific an action.] Some authorities maintain that the toxic element is a sapotoxin in the fruit, other

that it is due to a fungus *Gloeosporium periculosum* which grows on the fruit. A goat fed on the fruit and a calf which browsed on the leaves both became blind. [This fascinating question should certainly not be allowed to rest here. Investigation should not be difficult since animals are known to suffer in the same way (or apparently the same way) as human beings.] *H Harold Scott.*

ALLEN A. S. Pa Ping, or Kiating Paralysis *Chinese Med J* 1943 Oct.-Dec. v 61 No 4 296-301

Pa Ping is a better name than Kiating paralysis for this peculiar condition just as Mediterranean fever was better than Malta fever before the actual cause was determined for the giving of a limited local name may give a false impression of the area of prevalence of a disease. So now this disease is by no means limited to the Kiating district. Cases have been reported also from Wutung chiao Omei Chengtu Ipun Luhsien and elsewhere.

The author saw his first case in 1930 and later was himself attacked and since 1932 cases have been met with increasing frequency and he has now seen more than 200 cases. The symptoms are briefly these. Within a few hours of a meal there is a feeling of malaise and nausea and then almost sudden in onset there is a numbness and tingling of fingers and toes and in severe cases paralysis of arms and legs and the patient is unable to draw up the knees lift the arms or rise from his bed. Tactile sense is not affected nor are the sphincters involved. In mild cases these symptoms pass off in a few (four or five) hours, but in severe cases respiration becomes laboured, saliva drools from the mouth cyanosis develops and death occurs in 48 hours or less from cardiac and respiratory paralysis. Laboratory investigations give no clue. The fatality rate is 5-10 per cent.

Investigation has revealed that patients have increased in number since there has been increased activity in the salt producing area of China and the table salt in use in the areas where the disease occurs has been found to contain at times as much as 25 per cent of barium chloride. The author offers the surmise that the recent increase in prevalence is due either to change in the method of preparing the salt by which the barium which was formerly precipitated is now left in or to the tapping of a new well with high barium content. Treatment consists in early administration of sodium or magnesium sulphate to precipitate the barium as insoluble sulphate. Absorption of the chloride is rapid and the antidote should be given early.

[Experimental work recorded by KU YEK & LI in another contribution to this same issue of the *Chinese Medical Journal* shows that similar symptoms result from feeding animals (they used dogs and rabbits) with common salt containing barium chloride.] [See also the paper by KEH WEI HUANG below]

H Harold Scott

KEH WEI HUANG Pa Ping (Transient Paralysis simulating Family Periodic Paralysis) *Chinese Med J* 1943 Oct.-Dec v 61 No 4 305-12.

This is a record of twelve cases of Pa Ping a disease characterized by transient paralysis of the limbs. Their ages ranged between 20 and 50 years their occupations were very varied among them drivers merchants carpenter student and lawyer. All told of symptoms appearing soon after and related to a meal. One patient had had repeated attacks in the last six years another had three within six weeks. Before the onset of paralysis there were usually prodromata such as aching of muscles uneasiness in movement pain in arms and legs malaise nausea perhaps vomiting and diarrhoea. The paralysis would be present on waking during the night or in the early morning.

It is of a flaccid type and there is no sensory disturbance. Recovery was complete in all the twelve patients in four of them within 24 hours, and in none later than three days. The author speaks highly of the beneficial results following intravenous injection of 5 per cent. potassium citrate saying that rapid and complete recovery took place immediately after the injections [but where spontaneous recovery may be so rapid it is difficult to prove that the happy issue out of all their afflictions was *propter* and not merely *post* injections]. As regards the cause the author states "Chemical poisoning is suggested to be the possible cause and probably associated with the use of salt because the disease is limited to certain parts of Szechuen salt-producing areas."

H Harold Scott.

CHOU C. & CHEN Y C. The Absorption, Fate and Concentration in Serum of Barium in Acute Experimental Poisoning. *Chinese Med J* 1943, Oct.-Dec. v 61 No. 4 313-22 3 figs. (20 refs)

This study was instigated by the belief that the disease reported as Pa Ping in Szechuen was due to poisoning by barium chloride taken in table-salt. The authors carried out experimental work to test the effects of administering barium chloride to animals, mostly dogs by various routes—gastric tube intraperitoneal, intravenous, intramuscular and intradistal injection. This is therefore a pharmacological study the interesting aspect from the point of Pa Ping is the gastro-intestinal work. If the nature of the food was such as to precipitate the barium as sulphate absorption was little and slow otherwise it was rapid and could soon be detected in the serum for several hours. Its early reduction in amount in the blood would leave a residue too small to cause toxic symptoms. Symptoms of acute poisoning when the barium was given by mouth were salivation vomiting diarrhoea and tenesmus cardio-respiratory symptoms and tremors in isolated groups of muscles of extremities the form of twitchings and tremors in skeletal muscles first, followed by paralysis of the trunk then motor weakness of skeletal muscles first, followed by paralysis of the muscles of the legs then the trunk, then the arms. Thus the whole body might become paralysed but sensation was not lost. Barium was observed to be absorbed from the intestine not the stomach. Naturally if the barium was injected intravenously toxic cardiac effects were prominent—extra-systoles arrhythmia, tachycardia succeeded by bradycardia. It was rapidly removed from the blood stream, half of it within half-an-hour and 75 per cent. in two hours.

H Harold Scott.

STOKES, P H. Three Rather Unusual Cases. *E African Med J* 1944 Aug. v 21 No 8, 239-41

Three cases of rare pathological conditions in African natives are described
 Case 1 A male of the Jaluo tribe, aged about 30 was admitted to hospital in a semi-comatose state with marked retraction of the head and Kernig's sign strongly positive. His temperature was 102.8°F but had been 103°-104°F during the preceding three days his pulse was 88. Lumbar puncture showed the cerebrospinal fluid to be under increased pressure, but it was clear Malarial parasites were present in the blood. His illness was diagnosed as cerebral malaria and was treated accordingly. During the following week his temperature remained high but his cerebral symptoms improved. On the eighth day after admission typical mumps developed the cerebral symptoms are considered to have been caused by mumps, the presence of malarial parasites being merely incidental.

Case 2. A native of Uganda aged about 17 was admitted to hospital in January 1944 with his left leg below the knee and foot greatly swollen and tender his temperature was 102°F. There was no history of injury but the lame leg in the lower part and foot had been swollen on four occasions during the preceding three months and on two of these small abscesses had been opened. His leg was incised and explored but no pus was found. He was given prosectasine (benzylsulphanilamide) and leg baths and his temperature subsided and the swelling decreased. On February 3rd gangrene developed extending from the toes to the mid tarsal level and the leg became swollen and oedematous while his general condition was very toxic. The leg was amputated through the middle of the thigh and recovery was uneventful. No cause for the condition was discovered.

Case 3. This was a case of typical appendicitis generally regarded as rare in the African native. An editorial note states that 26 cases of appendicitis were operated upon in the Nairobi Native Hospital during 1943. J. F. Corson

GENERAL PROTOZOOLOGY AND PROTOZOAL DISEASES

ZUELZER W. W. Infantile Toxoplasmosis. With a Report of Three New Cases, including Two in which the Patients were Identical Twins. *Arch Pathology* 1944 July v 38 No 1 1-19 3 figs [24 refs.]

The author gives an account of three cases of infantile toxoplasmosis two of them in identical twins born of negro parents and the other in a white child. The cases of the twins one of which died at the age of one month the other still surviving at seven months were instances of intra uterine infection. The case in the white child terminated fatally at the age of 11 days. It is regarded as an instance of infection soon after birth. This is borne out by the character of the infection which was generalized throughout the body resembling acute infections in adults and by the fact that on two occasions the maternal blood failed to reveal protective antibodies when tested by Sabin's protection test in rabbits. In the twin that died the toxoplasms were much less numerous than in the acute case and the character of the lesions appeared to indicate that the acute phase of the disease had been passed *in utero*. The disease in the twins was in the chronic phase and was almost asymptomatic and had it not been for the post mortem diagnosis in the twin that died on the 11th day following its birth toxoplasmosis would not have been suspected in the surviving twin. In fact nystagmus at the seventh month was the first symptom to be noted. Blood taken from the mother of the twins was strongly protective in Sabin's test a further indication that infection of the twins had occurred before birth. In the case in the white child the main clinical features were convulsions opisthotonus instability of regulation of body heat and disturbances of respiration. The changes in the spinal fluid—xanthochromia mild pleocytosis and increased protein content—were similar to those reported from other cases of early infantile toxoplasmosis. The absence of hydrocephalus and calcification in the brain lesions can be accounted for by the short duration of the acute infection. Some degree of icterus was noted in the twins while extramedullary haemopoiesis was demonstrated in the tissues of the two fatal cases. It is considered that there is insufficient evidence to indicate that these two features are characteristic of toxoplasmosis.

The paper describes the three cases in considerable detail from the clinical and the pathological points of view and reviews much of the earlier literature on

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 infantile toxoplasmosis. It is undoubtedly a valuable contribution to knowledge of this relatively new disease of which barely three dozen cases have been placed on record. C M Wenyon

FRO L. G. The Incidence and Significance of *Trichomonas vaginalis* Infection in the Male. *Amer J Trop Med* 1944 May v 24 No 3 195-8.

At the Station Hospital at Fort George G Meade Maryland, over a period of seven months the early morning urethral discharge of 928 men who had been admitted for urethritis was examined for trichomonas. Of these men 735 were negroes and 191 were white. The 735 negroes gave 407 positive for the gonococcus and 121 positive for trichomonas. Only 18 were positive for both organisms while 189 showed neither. When the trichomonas-positive cases were grouped with the 189 non-specific ones it was revealed that 39 per cent. of the gonococcus-free subjects harboured trichomonas. Of the 191 white men 110 were positive for the gonococcus and 23 for trichomonas. It is noteworthy that the trichomonas subjects usually presented no symptoms the only complaint being a slight watery discharge. Of the total of 144 cases, 24 repeatedly revealed trichomonas over an observation period of one month. The discharge in these cases was of a dirty white or muco-purulent type. In stained smears of the discharge it was noted that the bacterial flora was similar to that seen in trichomonas vaginitis. In view of the fact that it has been established that *Trichomonas vaginalis* is easily implanted into the negative vagina it seems clear that the male is the important transmitter of the infection. C M Wenyon

GENERAL ENTOMOLOGY

LATES M. Notes on the Construction and Use of Stable Traps for Mosquito Studies. *J Nat Malaria Soc* Tallahassee Fla. 1944 June v 3 No. 2, 135-45 3 figs

When attempting to trap mosquitoes in the Egyptian Delta the author found that a large proportion of the mosquitoes entering the traps subsequently escaped through the vertically arranged baffle. He describes here the modifications introduced to overcome this. The ingress baffles were arranged in the horizontal plane so that the mosquitoes would have to fly downwards to escape. The trap was still more effective in the retention of mosquitoes if the edges of the baffle were of taut wire netting instead of wooden supports which served to make the opening more conspicuous. The traps were 2 m. long, 1 m. wide and 1.75 m. high so that they could hold a donkey or a man lying in a cot. The lower part of the trap on all sides was of wood plywood or galvanized iron the upper part screened with metal gauze. It is useful to place the trap on a cement platform surrounded by a shallow moat containing water to prevent the entrance of ants. Some results obtained in Egypt and in Colombia are given which illustrate how such traps can be used to measure preferences for different hosts and seasonal changes in abundance. V B Wigglesworth

CORREIA, R. R. & CERQUEIRA, F. M. C. Descrição de *Anopheles (Kertessia) lenaxus* nova espécie de anofelino do Campos do Jordão (Diptera Culicidae). [A Description of *A. lenaxus* New Species.] *Arquivos de Hig e Saúde Pública*. 1944 Jan., v 9 No 20 111-17 7 figs English summary p. 115

General Entomology

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KNIPLING E F GJULLIN C M & YATES W W A New Oil-Emulsion Mosquito Larvicide. U.S. Dept. Agric. Bur. Ent. Plant Quarantine E-587 1943 4 pp. [Summary taken from Dept. Scienc. & Indust. Res. Water Pollution Research Summary of Current Literature 1943 Aug v 16 No 8 231 Abstr. 922.]

The authors describe extensive field tests on the effectiveness of an oil emulsion larvicide against mosquito larvae in irrigated regions in overflow swales along the Columbia River in semi permanent ponds and roadside ditches and in mountain meadows 90-100 per cent. mortality was caused in 24 hours when a mixture containing 1 part of Diesel oil with 4 per cent. emulsifier and 6-9 parts of water was applied as a spray at a rate of 4 gal. per acre. The emulsifier consisted of sulphated sperm oil (Nopco 1216) or a phthalic glyceryl alkyl resin (B 1956) or a complex amine with a chain of 18 carbon atoms (Amine 230 Y).

WILSON C S MATHIESON D R & JACHOWSKI L A Ingested Thiamin Chloride as a Mosquito Repellent Science 1944 Aug 18 147

As thiamin chloride had been reported (SHANNON Minnesota Med 1943 v 26 799) to relieve the itching of mosquito bites and to prevent further biting the authors made experiments to test these statements. The doses of thiamin chloride taken by the volunteers varied in different experiments 505 mgm were taken in three days 100 mgm were taken and then the volunteer exercised to produce sweating one arm being covered with indalone (n butyl mesityl oxide oxalate) as a control three persons took 30 mgm four times a day for three days Tests were made with *Aedes aegypti* in all the experiments but no repellent action was found Subsequent tests by the U.S. Department of Agriculture and by the National Institute of Health have confirmed these results. J F Corson

MADDERN A H LINDQUIST A W & KNIPLING, E F Tests of Repellents against Chiggers. J Econom Entom 1944 Apr v 37 No 2 283-6

Tests on a series of repellents were made under field conditions against chiggers [that is mites of the genus *Trombicula* and its allies known variously as harvest bugs bête rouge Itch mites etc.] Such repellents proved more effective and lasting when applied to the clothing than to the skin The most practical means of treating the clothing is to apply the liquid repellent from a narrow mouthed bottle in a half inch band around the inside of the waist the fly and the bottoms of the legs of the trousers the cuffs fly and neck of the shirt and in a wide band around the upper part of the socks The most successful materials were the proprietary repellents Indalone (n butyl mesityl oxide oxalate) and Rutgers 612 (2-ethylhexane diol 1 3) and dimethyl phthalate. These gave good protection up to 30 days after treatment For cheapness availability and desirability for use the authors recommend dimethyl phthalate [a colourless and almost odourless oily liquid] V B Wigglesworth

CARTER H F WREDD G & D ABRERA V St E. The Occurrence of Mites (Acarina) in Human Sputum and their possible Significance Indian Med Gaz 1944 Apr v 79 No 4 163-8 [13 refs.]

The occurrence of mites in the sputum of 17 out of 28 persons suffering from respiratory disorders (including asthma and chronic bronchitis) is recorded. The observations were made in Ceylon where most of the subjects had resided for a few months only The mites were of at least ten species those identified were the common species present in stored products and debris of various kinds

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such as species of *Tyroglyphus*, *Carpoglyphus*, *Glyphoglyphus*, *Chyletus* and *Tarsonemus*. Such mites were common in the hospital wards and in some cases were proved to be air borne but elaborate precautions were taken to exclude the possibility of accidental contamination of the sputum and washings from the nose and mouth proved negative. The authors therefore conclude that the mites did actually come from the lungs and bronchi in one case at least there was evidence that the mites had adapted themselves to the conditions there and were breeding. They believe that the chief method of infection is by inhalation and that infestation may have been of prolonged duration in some cases. They put forward the view that the condition variously known as "pseudo-tuberculosis", eosinophil lung, tropical eosinophilia, etc. may in part at least be due to mite infestation of the respiratory system. The numbers of mites present were diminished and the pulmonary symptoms were improved, after treatment with organic arsenicals. In three of the mite-infested patients there was a high degree of eosinophilia, which was reduced after treatment with arsenic. An analogous condition occurs in monkeys and is (at all events) far from uncommon in antopuses on Rhodes monkeys at the Zoological Gardens London.]

PACKHAMIAN A. An Apparatus to facilitate the Feeding of Insects on Laboratory Animals. *Amer J Trop Med* 1944 July v 24 No 4 273-5 4 figs.

LABORATORY PROCEDURES

STEINER, G. & STEINER, Grete. New Simple Silver Stain for Demonstration of Bacteria, Spirochetes, and Fungi in Sections from Paraffin-Embedded Tissue Blocks. *J Lab & Clin Med*. 1944 Aug v 29 No 8, 868-71

For success with the method described tissues are fixed in formalin. Zenker fixation cannot be used nor can celloidin films. The authors have used their method for the past three years and have found it perfectly satisfactory. The details of the staining process are: The sections 6-7 μ thick, after removal of the paraffin in the usual way are placed in 1 per cent. uranum nitrate for three hours then washed twice in distilled water after which they are immersed in 1 per cent aqueous silver nitrate and kept for two hours at 58-58° in the over and again thoroughly washed in distilled water. Next, after dehydration in graded alcohols the sections are placed for five minutes in 2.5 per cent. gum mastic in absolute alcohol. Without washing, they are transferred directly to hydroquinone for reduction till the colour of the sections becomes a light brown (usually 12-15 minutes) they are then washed three times in distilled water and dehydrated, cleared and mounted.

To obtain satisfactory results certain precautions are necessary. The reducing solution consists of 1 gm. hydroquinone dissolved in 60 cc. distilled water to this are added 20 cc. of the 2.5 per cent. gum mastic in absolute alcohol and 20 cc. of silver nitrate sodium potassium tartrate solution. Details for preparing the last are given as follows:—

Two gm. of silver nitrate are dissolved in 1 000 cc. of boiling distilled water. When the chemical is dissolved and the water is boiling 1.65 gm. of powdered sodium potassium tartrate is quickly added until the white precipitate changes to grey. Then the solution is filtered while hot into an amber bottle with glass stopper. The silver nitrate sodium potassium tartrate solution is poured into the alcoholic gum mastic solution and not vice versa. equal parts 20 cc. each, of silver nitrate sodium potassium tartrate solution and of 2.5 per cent alcoholic gum mastic solution are used.

The hydroquinone solution must be freshly prepared each time the other solutions keep indefinitely as stock
All glassware must be rinsed in distilled water before use and the dish for the gum mastic solution rinsed with absolute alcohol The total time taken is under 2½ hours during two hours of which the slides are in the oven and the technician can get on with other work.

Bacteria spirochaetes and fungi present a black mirror like appearance showing up on the yellow or brown tissue elements It is claimed that there is no precipitation of metallic silver and that the sections do not show artefacts

H Harold Scott

REPORTS SURVEYS AND MISCELLANEOUS PAPERS

SHROOZET Ed Rapport sur le fonctionnement de l'Institut Pasteur d'Algérie en 1943 [Report on the Pasteur Institute, Algeria for 1943.] Arch Inst. Pasteur d'Algérie 1944 Mar v 22, No 1 63-99 [24 cols]

LEDEBT H La dépopulation chez les Nkundo (Depopulation in the Nkundo Tribe.) Rec. Travaux Sci Méd Congo Belge Léopoldville 1944 Jan. No 2 130-40

Investigations were made to find the cause of the relatively small number of children in the population of two areas 45 and 67 kilometres respectively from Coquilhatville in the Belgian Congo. One of the areas Indjolo had a population of 1,340 of the Nkundo tribe living in 10 villages and 348 pigmies in three villages the other area Bofidji Est had 1,602 Nkundos in 19 villages and 74 pigmies in two villages In Indjolo the ratio of Nkundo children to adult females was 0.36 to 1 the figure for the pigmies being 1.5 to 1 in Bofidji Est the respective figures were 0.46 and 1.32. Diseases to be considered as possible causes of the low fertility among the Nkundos were gonorrhoea syphilis trypanosomiasis yaws and leprosy. An examination of adult males showed that gonorrhoea could be excluded as a cause. The tests for syphilis included the Wassermann Meinicke and Kahn reactions for both blood serum and cerebrospinal fluid and the latter was also examined by the Weichrodt and Pandey tests and by cell count and total protein estimations. Evidence of syphilis was found in 60 per cent of the Nkundo and nearly one-third of these showed signs of neurosyphilis. In trypanosomiasis the cell count of the cerebrospinal fluid is frequently high over 50 cells per cmm. and is closely associated with increased total protein content in the present cases the cell count was usually below 50 and the number of persons with altered cerebrospinal fluid was 3 to 10 times the number of persons suffering from trypanosomiasis. An excess of total protein was more frequently found than an excess of cells. It was considered that yaws and leprosy could be dismissed as causes of infertility. The author concludes that old standing latent syphilis was responsible for the small proportion of children in the Nkundo tribe. The pigmies also showed evidence of a high incidence of syphilis yet the proportion of children among them was much greater this is attributed to their stricter sexual life compared with the promiscuous habits of the Nkundo the effect being that the non-syphilitic pigmies maintain the numbers of the population J F Corson

brightness correspondingly less. Indirect glare in rooms can be prevented by arranging screens of vegetation to protect windows.
Plans are given of suggested layouts for houses and for estates.
T Bedford

MITSCHERLICH, E. Stallbauten in warmen Ländern. [Animal Houses in Hot Countries.] *Dtsch. Tropenmed. Zeitschr.* 1943 Nov 1 v 47 No. 21/22, 578-62 10 figs. [Numerous refs.]

This paper deals with the construction, ventilation, siting and other matters of importance in relation to cattle-sheds, stables, sheep and goat sheds, pigstyes and hen-houses.

BOOK REVIEWS.

GELFAND M [MB ChB, M.R.C.P D.M.R. etc.] *The Sick African. A Clinical Study* With a Foreword by Colonel A. P. MARTIN O.B.E. MD D.P.H. D.T.M. & H. etc. 373 pp. With 123 figs. on 78 pls. & 3 diagrams. 1944 Cape Town Post-Graduate Press in association with the Stewart Printing Co. (Pty) Ltd. Carlton House Alfred Street [25s.]

This book is primarily intended for members of the medical profession, though as the author rightly hopes, missionaries and medical orderlies will find it helpful, provided that they have a sound theoretical knowledge and some practical experience of sickness in the African or any other.

Though the author has only had a few years' experience and that confined to Southern Rhodesia, he has an African background, and it is refreshing to find a graduate of the Cape Town Medical School insisting that not only the utilitarian but also from the humanitarian viewpoint, an adequate native medical service is an inescapable obligation. He believes that education and Christianity are important factors, and rightly emphasizes that the local training of nurses midwives orderlies and "even doctors" (the latter to be restricted to a Government Service for Natives) is the only practical solution.

Vast and divergent as the African continent is, it is nevertheless possible to generalize, and pathology is very similar throughout with the possible exception of deficiency diseases which, fortunately, are much rarer in the tropical forest area than elsewhere.

The opening chapters on "The Patient" and "The Examination" are helpful in indicating what to look for and what not to expect. One does not quite agree that the native is a fatalist. He refuses to accept disease and death as part of the ordained natural order and insists in smelling out the witch and bringing him to book with the help of his M.O.H. the witch doctor. The author recognizes however that it is not the intrinsic problem, but lack of funds and facilities which make it difficult adequately to treat the sick African.

The chapters on various diseases or systemic affections are very readable and well-arranged, though a slightly more distinctive type for the sub-headings would improve the form. Much attention is usefully given to differential diagnosis but treatment is usually somewhat condensed.

Book Reviews

Vol. 42. No 1]

For the sake of completeness a little rather unnecessary matter has been inserted such as that on congenital heart disease and the localization of cerebral tumours

The reviewer agrees with nearly all the factual statements though a few opinions seem a little too dogmatically stated e.g. that crawl-craw is probably a form of scabies and that tropical myositis is rare in Europeans

One is glad to see emphasized the fact that tuberculosis control is really more important than a leprosy campaign. A brief warning might be introduced in regard to the treatment of bilharzia by injection of tartar emetic as to the danger of lighting up tuberculous lesions in the lungs especially in view of the author's pessimistic verdict that he has never seen a native recover from phthisis. He will see this eventually. He will also see ground itch in the feet of riverine tribes.

Subsequent editions of this book will no doubt be called for and will include the use of benzyl benzoate for scabies DDT for the prophylaxis of louse borne disease the use of spraying methods in the control of mosquitoes and the latest about the sulpha drugs

There are remarkably few misprints or mis spellings. Illustrations are numerous sometimes duplicated but their grouping renders them less valuable as aids to the text. References are few and not widely representative and might be omitted without disadvantage

C C Chesterman

SOPER Fred L. WILSON D Bruce LIMA Servulo & ANTUNES Waldemar Sá.
The Organization of Permanent Naiton-Wide Anti-Aedes aegypti Measures
in Brazil. 137 pp. With 27 figs. (9 on 5 pls.) & 2 maps. 1943 New
York The Rockefeller Foundation

In the review of this publication [this Bulletin 1944 \ 41 689 it was remarked that the price was not mentioned. The Bureau is now informed that the volume is a Rockefeller Foundation publication intended for free distribution to those persons especially interested in or responsible for the control of *Aedes aegypti*. A simple request to the Foundation from interested persons is all that is necessary

COCKER Dorothy E. (S.R.N. S.C.M. etc.) Aids to Tropical Nursing. With a Foreword by L. N. NAPIER C.I.E. F.R.C.P. (Lond.) Director School of Tropical Medicine Calcutta pp viii+159 12 figs. 1944 London Baillière Tindall & Cox 7 & 8 Henrietta Street Covent Garden W.C.2. [4s.]

The aim of the editors of the *Aids to Nursing* series of text-books is to produce handy volumes on different branches of nursing which will serve as accurate text books for the student nurse and which will also take their place in an up-to-date reference library for the personal use of the qualified nurse.

The authors are sister tutors in the more important teaching hospitals and in the preparation of the series the collaboration of doctors with expert knowledge of the different subjects has been secured.

The volume on tropical nursing appears likely to be particularly valuable to nurses in Britain who are intending to go out to the tropics. A short introductory section deals with personal hygiene and gives very practical advice on the rules for the maintenance of health in hot climates. The author is indeed a firm disciplinarian on the subject of indulgence in food and drink in the tropics. Those who hanker after the flesh pots receive short shrift from her. Some

people in hot climates habitually over-eat and obese, ungainly figures are a common sight." Nor is she a supporter of the stay-me-with-flagons school of thought. Drinking alcohol as a regular habit is not good—those who are used to taking a fair amount are liable to be victims of heat-stroke and the complications following malaria.

In the next short section the disorders due to climate are clearly described. The bulk of the book deals—in alphabetical order—with the more important tropical diseases. The promise of the title is well fulfilled by the detailed attention paid to the nursing care which should be given in each disease. Their prophylaxis, however, is only briefly considered. More space might, with advantage, be devoted to the preventive aspect in subsequent editions. Further instruction would also be useful about tropical foods and the dietetic needs of the various peoples in the tropics for it is chiefly among them that most nurses will subsequently be working.

The publication of this book is very opportune since the need for special courses for nurses going to the tropics has now been recognized. This text book can be recommended to them with confidence as a concise and accurate account of the clinical aspects of tropical nursing.

M G Blacklock.

TROPICAL DISEASES BULLETIN

1945

Vol 42]

No 2

SUMMARY OF RECENT ABSTRACTS *

II YELLOW FEVER

Epidemiology

KIRK (p 121) has contributed an account of the outbreak of yellow fever which occurred in the Sudan in 1940 in relation to the epidemiology of the disease in Africa as a whole and to its spread and control. The virus may be present in places where there is no evidence of active disease and yet where practically the whole population is immune within the endemic area however rural outbreaks may occur (as in the Sudan) but spread may also take place by gradual extension of the present endemic area in the absence at first of any noticeable epidemic of recognized cases. This paper should be read in original by those interested in yellow fever in Africa.

A viscerotomy service has been in operation in the Belgian Congo since 1938 and has disclosed six cases of yellow fever from widely separated areas in a total of 4,340 examinations. LIEGROIS (p 102) considers that these were probably cases of jungle yellow fever because in spite of search and protection tests it was impossible to find other cases in their vicinity and it is therefore difficult to explain their occurrence except by the assumption that there was some reservoir of infection other than man. Protection tests have been carried out with sera from all parts and in certain areas (which are named) there is evidence of recent disease in that the sera of children are not uncommonly positive. In other parts of the country no evidence of immunity was found. CECCALDI (p 846) reports on the yellow fever activities of the Pasteur Institute of Brazzaville during 1942. Vaccinations were carried out and test of sera made the account is of more local than general interest.

Immune bodies to the yellow fever virus have been found in monkeys and other animals from Africa. The evidence suggests that monkeys may be reservoirs of infection but monkeys are not known to travel far and it occurs to FINDLAY and COCKBURN (p 122) that birds might act in this capacity and if it can be established that these bodies are the result of infection with the virus the findings may throw light on the maintenance of the disease. The authors note however that protective bodies have been found in domestic animals from areas in which yellow fever is not known to exist.

*The information from which this series of summaries has been compiled is given in abstracts which have appeared in the *Tropical Diseases Bulletin* 1944 v 41. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

SMITH *et al.* (p. 210) reviewing the results of histological liver examination and of protection tests carried out in Colombia in recent years, conclude that the jungle type of yellow fever is probably continuously present in certain areas of the country. On the other hand with the exception of one very small epidemic in Buenavista Caldas in 1937 no instance of yellow fever transmitted by *Aedes argyph* has been observed in Colombia since 1929.

As a result of careful investigation of jungle yellow fever in Colombia, BUCHER *et al.* (p. 475) have been able to present a very full account of the epizootology and epidemiology of the disease. The disease is transmitted among forest animals by *Haemagogus capricornis* an arboreal mosquito which has been proved a vector by bite and which has been found infected in nature. *Haemagogus capricornis* may survive the dry season in the tree tops and infected mosquitoes may carry the virus into the next breeding season at the beginning of the rains. No virus has been found in larvae collected in this study. *Aedes leucocelaenus* has also been found infected in nature and it is possible that *Aedes fluviatilis* and *Aedes scapularis* may also play a part. Of the forest animals in which the disease is maintained, only primates and marsupials are important though other animals have been found to be immune. The primates and marsupials are arboreal in habit. In them virus is present in the blood for a few days only; the animals do not suffer any important illness, but develop antibodies within a short time and then become permanently immune. In an immune community explosive outbreaks such as occur in non-immune communities do not take place. The movements of infected animals are not seriously impeded, and their migration can play an important part in spreading the disease. Man becomes infected when in contact with the forest *Haemagogus* acting as vector from animal to man, but if the human population is dense *Haemagogus* may act as vector from man to man.

BATES (p. 749) has extended the earlier work of BUCHER *et al.* on the susceptibility of marsupials to yellow fever virus. Details of the experiments should be sought in the original, but the author admits that it is difficult to form an opinion of the importance of these animals in the epidemiology and epizootology of jungle yellow fever.

The results of a large survey of human blood samples, by the intraperitoneal mouse protection test in areas extending from Mexico to Colombia lead to the conclusion that in recent years endemic yellow fever has been restricted to Eastern Panama (KUNN and CRAWFORD p. 123).

POTENZA (p. 478) reports that no evidence of yellow fever was found in the necrotoomy service of Venezuela between 1937 and 1940.

Aetiology Transmission

The ordinary Aasi strain of yellow fever virus could not be established in young chicks by intracerebral inoculation but LARMONET and MOUSSATCHE (p. 123) have succeeded in establishing in this fashion a strain which had grown in tissue culture and subsequently been passaged in developing fowl embryos. The strain lost its viscerotropism for rhesus monkeys but not its neurotropism on intracerebral injection into these animals.

BATES and WEIR (p. 747) LARMONET (p. 747) and BATES (p. 749) report on experiments in which tests of susceptibility to yellow fever virus were made in cane rats, marmosets and *Saimiri* monkeys respectively. This work is interesting from the point of view of laboratory animals but the details of the results should be sought in the original papers.

DR ASSUMPTION (p. 836) has demonstrated cross protection between a strain of classical neurotropic yellow fever virus and two strains of jungle yellow fever virus.

KOPROWSKI and LENNETTE (p 1030) have shown that addition of sulphapyridine or sulphathiazole to tissue cultures does not interfere with the propagation of yellow fever virus suitable concentrations of the drugs could aid direct isolation of the virus by their action against bacterial contaminants. The same authors (p 1030) have shown that these drugs have no therapeutic value in infected mice and that they do not prevent propagation of the virus in developing fowl embryos.

LEWIS (p 278) has found *Aedes aegypti* widely distributed in Eritrea up to a height of about 1650 metres. Several other potential vectors of yellow fever were also found.

LEWIS (p 213) has noticed that small water tortoises found in some water jars in the Sudan feed voraciously on mosquito larvae and that the larvae of *Aedes aegypti* were not found in such jars though present in others in which there were no tortoises.

BATES (p 936) considers that *Haemagogus capricornis* which is found in the forest canopy of Colombia is kept in the tree tops by a response to the humidity gradient an avoidance of the zones with a relative humidity of 85 per cent. It becomes more abundant at ground level in open dry localities or after a succession of clear days. This mosquito has a single diurnal peak of activity around midday.

Control Vaccination

Investigation the complement fixation test in yellow fever LENNETTE and PERLOWAGORA (p 211) have overcome the difficulty of procuring a suitable antigen by making use of techniques found satisfactory in similar work with other viruses which are described in detail. They find that the test in which the antigen is derived from infected mouse brain is specific. In monkeys complement fixing antibodies are found in the blood at the end of the second week after infection reaching a maximum about the third week and thereafter gradually disappearing. In persons vaccinated with 17 D if there was no post vaccination reaction the antibodies occurred in only about 20 per cent. If there was a severe reaction the antibodies were present in up to 80 per cent of subjects. Natural yellow fever was followed by a high antibody rate. This test is of no value for the routine checking of post vaccination results but may be very useful in field immunity surveys since the relatively rapid disappearance of complement fixing antibodies from the blood after infection indicates that if these bodies are present the infection must have been fairly recent. Wassermann positive sera tend to give non-specific reactions which can usually be avoided by inactivation of the sera at 65°C.

In the *Boi Oficina Sanitaria Panamericana* (p 212) is a brief statement of the record of the Brazilian Government and the Rockefeller Foundation in eliminating *Aedes aegypti* from several of the States of Brazil. Reference is also made to the extensive viscerotomy service which has been established and to the large vaccination campaign undertaken.

BUGHER and GAST-GALVIS (p 478) review the evidence of the protective action of yellow fever vaccine in Colombia by quoting figures which show that in exposed populations the disease practically never occurred in persons who had been vaccinated though a considerable number of cases were found in those who had not. Even in vaccinated persons whose sera no longer showed protective substances by the mouse protection test no cases were found but although this probably indicates some residual immunity it is probably wise to re-vaccinate such persons. The evidence of protection conferred by the vaccine is very convincing.

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FOX and PENNA (p. 125) have studied the behaviour of vaccine virus 17D in *rhesus* monkeys as observed during the routine control of individual batches of the vaccine. The quantity of virus in the intracerebral inoculum is related to occurrence of circulating virus, and of serum antibodies and to the onset and duration of the febrile reaction: the larger the dose, the earlier the appearance of virus, antibodies and fever.

Experience in Brazil had shown that certain batches of vaccine virus 17D had failed to give adequate protection, whereas with other batches the result was satisfactory. The batches which failed had been prepared from virus at the 705th to 391st subculture, the satisfactory batches from virus at the 229th to 253rd subcultures. BERGER and SMITH (p. 477) investigated the matter and found that high subcultures did not in themselves necessarily produce loss of immunizing power. It was then thought that the pools of human serum used in culture which had been taken from persons in Brazil, may have contained specific antibodies too weak to have been detected by the protection test then in use and that the virus growing in contact with these antibodies might on this account have suffered a reduction in antigenic power. Tests were therefore made, with parallel controls, by culturing 17D through 57 passages, in contact with specific antibodies barely insufficient to prevent multiplication and by titration of the protective bodies produced by inoculation of various doses of these strains in human volunteers. No significant differences could be found, and it is therefore concluded that growth of the virus in the presence of such amounts of antibody does not affect antigenic power as measured by a mouse protection test.

SWARTZ (p. 278) reports a severe constitutional allergic reaction in a man who had received an injection of yellow fever vaccine. He was found to be sensitive to egg and fowl tissues, and it is thought that as the vaccine had been prepared from inoculated eggs, this fact explained the reaction.

SAWYER *et al.* (p. 1025) have contributed a lengthy and comprehensive study of jaundice in men of the United States forces vaccinated against yellow fever. The interest lies, of course, in the hepatitis since it has conclusively been shown that the yellow fever virus itself was not the cause of the condition. The vaccine is no longer prepared in a medium containing human serum, and hepatitis should not occur. These papers contain very full discussions of the relevant problems. TURNER *et al.* (p. 750) report on a considerable outbreak of hepatitis in United States troops who had been inoculated with scterogenic yellow fever vaccine. There is of course, no suggestion that the disease was in any way related to yellow fever. FINDLAY *et al.* (p. 1028) give a description of 670 cases of hepatitis after yellow fever vaccination, in West Africa, and consider in detail the clinical, epidemiological and immunological data. Here again the yellow fever interest is incidental. JONES and MACRER (p. 809) have failed to produce jaundice in horses by injection of scterogenic yellow fever vaccine. The virus of yellow fever could not be detected in the serum of the horses after the inoculations.

Charles Wilcocks

MALARIA

COLLIER Jean M. A Case of Malaria acquired near Sydney, New South Wales. *Med J Australia* 1944 Aug 28 v 2 No 9 213-14

WOLPERS C. Zur elektronenoptischen Darstellung der Malaria tertiana. [The Parasite of Tertian Malaria under the Electron Microscope.] *Klin Woch* 1942 Nov 28 v 21 No 48 1049-54 12 figs [18 refs]

The author who has been studying the benign tertian malarial parasite —*P. vivax*—by means of the electron microscope gives in this paper an account of his observations and the methods he has employed in making them. The work is highly technical and has involved a preliminary study of normal erythrocytes by special methods. It is admitted that the interpretation of the appearance of the malarial parasites is very difficult nevertheless the following conclusions have been drawn. At a very early stage in the invasion of an erythrocyte by a malarial parasite diffuse changes occur in the membrane of the cell, while the haemoglobin altered in some way is deposited on the membrane in discrete masses representing Schüffner's dots. Later stages of the parasite can be seen to be anchored to the cell membrane by claw like processes. When schizogony commences the lipoids of the cell membrane are absorbed by the parasite and deposited on the surface of the merozoites as a protective covering. When the merozoite penetrates an erythrocyte the lipoidal covering is discarded the parasite continuing its growth within the erythrocyte without any protective sheath. The various appearances described in the paper are illustrated by a dozen micro-photographs. C M Wenyon

RUGE H & KREMER H. Morphologische Änderung der Malaria Parasiten bei Atebrinprophylaxe. [Morphological Changes in the Malarial Parasite under Atebrin Prophylaxis.] *Ztschr f Hyg u Infektionskr* 1942 Dec 31 v 124 No 5 441-51 20 coloured figs on 1 folding pl [20 refs]

Various observers have studied the changes undergone by malarial parasites during atebryn treatment but no one has attempted hitherto to gauge the effect on the parasites of the drug when taken prophylactically in daily doses varying from 0.03 to 0.06 gm. With these daily doses the authors report that at a certain field station they were able to study the malarial parasites in 200 cases of malaria which had occurred in spite of the prophylactic atebryn. In these cases it was noted that many but not all of the parasites were abnormal in appearance owing to changes which had occurred in the cytoplasm and chromatin. Unlike the effect of atebryn when administered in the larger therapeutic doses which bring about changes in the pigment this material is little altered by the quantity given in prophylaxis. As regards the changes in the cytoplasm there are formation of vacuoles irregularities in staining clumping notching formation of processes and assumption of a stellate form. The chromatin tends to break up into a varying number of fragments which are distributed throughout the cell and may become vacuolated. The various abnormalities described in the paper are illustrated in a coloured plate in which twenty infected red blood corpuscles are depicted. The changes produced render identification of the parasites especially in thick films a difficult matter. C M Wenyon

PURI I M. Synoptic Tables for the Identification of the Full-Grown Larvae of the Indian Anopheline Mosquitoes. 4th edition (revised) *Health Bull No 16 (Malaria Bureau No 7)* 109 pp 83 figs. [Summary taken from *Rev Applied Entom.* Ser B 1944 Oct v 32 Pt 10 182.]

In this revision of a bulletin already noticed the advanced key that forms part of the early editions is omitted and only one main key is given including

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Experience in Brazil had shown that certain batches of vaccine virus 17D had failed to give adequate protection, whereas with other batches the result was satisfactory. The batches which failed had been prepared from virus at the 305th to 391st subculture: the satisfactory batches from virus at the 229th to 235th subcultures. BUCHER and SMITH (p. 477) investigated the matter and found that high subcultures did not in themselves necessarily produce loss of immunizing power. It was then thought that the pools of human serum used in culture which had been taken from persons in Brazil, may have contained specific antibodies too weak to have been detected by the protection test then in use and that the virus growing in contact with these antibodies might on this account have suffered a reduction in antigenic power. Tests were therefore made with parallel controls by culturing 17D through 57 passages in contact with specific antibodies barely insufficient to prevent multiplication and by titration of the protective bodies produced by inoculation of various doses of these strains in human volunteers. No significant differences could be found, and it is therefore concluded that growth of the virus in the presence of such amounts of antibody does not affect antigenic power as measured by the mouse protection test.

SWARTZ (p. 278) reports a severe constitutional allergic reaction in a man who had received an injection of yellow fever vaccine. He was found to be sensitive to egg and fowl tissues and it is thought that as the vaccine had been prepared from inoculated eggs this fact explained the reaction.

SAWYER *et al.* (p. 1023) have contributed a lengthy and comprehensive study of jaundice in men of the United States forces vaccinated against yellow fever. The interest lies of course in the hepatitis since it has conclusively been shown that the yellow fever virus itself was not the cause of the condition. The vaccine is no longer prepared in a medium containing human serum, and hepatitis should not occur. These papers contain very full discussions of the relevant problems. TURNER *et al.* (p. 750) report on a considerable outbreak of hepatitis in United States troops who had been inoculated with heterogenic yellow fever vaccine. There is of course, no suggestion that the disease was in any way related to yellow fever. FURSLAY *et al.* (p. 1028) give a description of 670 cases of hepatitis after yellow fever vaccination, in West Africa, and consider in detail the clinical, epidemiological and immunological data. Here again the yellow fever interest is incidental. JONES and MATHER (p. 839) have failed to produce jaundice in horses by injection of heterogenic yellow fever vaccine. The virus of yellow fever could not be detected in the serum of the horses after the inoculations.

Charles Wilcocks.

MALARIA

COLLIER, Jean M. A Case of Malaria acquired near Sydney, New South Wales. *Med J Australia* 1944 Aug 26 \ 2 No 9 213-14

WOLPERS C. Zur elektronenoptischen Darstellung der Malaria tertiana. [The Parasite of Tertian Malaria under the Electron Microscope.] *Klin Woch* 1942 Nov 28 \ 21 No 48 1049-54 12 figs [15 refs]

The author who has been studying the benign tertian malarial parasite —*P. vivax*—by means of the electron microscope gives in this paper an account of his observations and the methods he has employed in making them. The work is highly technical and has involved a preliminary study of normal erythrocytes by special methods. It is admitted that the interpretation of the appearance of the malarial parasites is very difficult nevertheless the following conclusions have been drawn. At a very early stage in the invasion of an erythrocyte by a malarial parasite diffuse changes occur in the membrane of the cell while the haemoglobin altered in some way is deposited on the membrane in discrete masses representing Schullner's dots. Later stages of the parasite can be seen to be anchored to the cell membrane by claw like processes. When schizogony commences the lipoids of the cell membrane are absorbed by the parasite and deposited on the surface of the merozoites as a protective covering. When the merozoite penetrates an erythrocyte the lipoidal covering is discarded the parasite continuing its growth within the erythrocyte without any protective sheath. The various appearances described in the paper are illustrated by a dozen micro-photographs. (C. M. Henson)

RUGG H & KRESLER, H. Morphologische Änderung der Malariparasiten bei Atebrinprophylaxe. [Morphological Changes in the Malarial Parasite under Atebrin Prophylaxis.] *Ztschr f Hyg u Infektionskr* 1942 Dec 31 \ 124 No 5 441-51 20 coloured figs on 1 folding pl. 20 refs

Various observers have studied the changes undergone by malarial parasites during atebrian treatment but no one has attempted hitherto to gauge the effect on the parasites of the drug when taken prophylactically in daily doses varying from 0.03 to 0.08 gm. With these daily doses the authors report that at a certain field station they were able to study the malarial parasites in 24 cases of malaria which had occurred in spite of the prophylactic atebrian. In these cases it was noted that many but not all of the parasites were abnormal in appearance owing to changes which had occurred in the cytoplasm and chromatin. Unlike the effect of atebrian when administered in the large therapeutic doses which bring about changes in the pigment this material is little altered by the quantity given in prophylaxis. As regards the changes in the cytoplasm there are formation of vacuoles irregularities in staining clumping notching formation of processes and assumption of a stellate form. The chromatin tends to break up into a varying number of fragments which are distributed throughout the cell and may become vacuolated. The various abnormalities described in the paper are illustrated in a coloured plate in which twenty infected red blood corpuscles are depicted. The changes produced render identification of the parasites especially in thick films a difficult matter. (C. M. Henson)

PUGH I M. Synoptic Tables for the Identification of the Full-Grown Larvae of the Indian Anopheeline Mosquitoes. 4th edition (revised). *Health Bull* No 16 (Malaria Bureau No 7) 109 pp 83 figs. [Summary taken from *Rev Applied Entom* Ser B 1944 Oct \ 32 Pt 10 182.]

In this revision of a bulletin already noticed the advanced key that forms part of the early editions is omitted and only one main key is given including

[February 1945]

all the species of *Anopheles* recorded from India, Burma and Baluchistan of which the larvae are known. In place of the advanced key there are supplementary notes on the various species with keys to varieties. Some alterations have been made in the main key to simplify its use. As there are certain species that appear to be restricted to particular areas, five separate keys are given for Baluchistan North-West Frontier Province and Sind, Delhi Province and the Punjab, Central India and Rajputana, Peninsular India and the United Provinces and Eastern India and Burma. These geographical divisions are purely arbitrary. Characters found to differentiate a large majority of the larvae of *A. candidus* Redw and *A. subpictus* Grass are incorporated for the first time.

- i. COCHRANE E. Is *A. argyritarsis* a Malarial Vector in Grenada? *Caribbean Med. J.* 1941 v 3 No 4 183-5
- ii. — Notes on *A. argyritarsis* and *A. pseudopunctipennis* in Grenada. *Ibid.* 1942 v 4 No 3 97-100

EARLE (this Bulletin 1934 v 31 631) concluded that *Anopheles aequalis* (*A. ferrimaculatus*) was the chief if not the only carrier of malaria in Grenada. *A. argyritarsis* was easily infected in the laboratory but was not an important vector of malaria though it might be contributory along with *A. aequalis*. The third species, *A. pseudopunctipennis* present in Grenada, was probably not a carrier.

i. An outbreak of subtertian malaria in 1938, in a population of about 600 living along the bank of the St. John's river led to a thorough search for larvae in the locality. No larvae of *A. aequalis* were found within a radius of three miles from the river but larvae of *A. argyritarsis* and *A. pseudopunctipennis* were numerous.

ii. A further study of *A. argyritarsis* and *A. pseudopunctipennis* was made. 119 specimens of *A. argyritarsis* out of 134 caught in three months were dissected none being found infected. Of 1011 specimens of *A. pseudopunctipennis* caught in stables 932 were dissected with negative results. A decline in the incidence of malaria in this locality coincided with a scarcity of *A. argyritarsis*. *A. aequalis* was found breeding there on one occasion only. The author apparently considers that *A. argyritarsis* may be more important as a vector of malaria than it has been thought to be.

J F Corson

- URTI O. Resistência de ovos de algumas anofelinas de São Paulo. [Resistência of Eggs of *Anopheles* of São Paulo.] *Arquivos de Hig. e Saúde Pública*. São Paulo 1943 Sept v 8 No 19 85-72 English summary

The observations recorded concern the eggs of *A. albistarsis*, *A. nordestensis* and *A. strobilator*. Eggs kept in the laboratory on moist or dry filter paper remained viable from two to eight days in the winter this period was prolonged to 10 and exceptionally to 15 days. Eggs were also kept in more or less natural conditions, in receptacles containing moist earth from the natural breeding places the receptacles were kept in the open air. From the fourth day onwards rain water was added in quantity sufficient to keep the earth submerged. In these conditions the eggs remained viable from 4 to 15 days in both summer and winter.

Norman White

- URTI O. Origêmo dos focos de anofelias de São Paulo. [Dissolved Oxygen in Water of *Anopheles* Breeding Places in São Paulo.] *Arquivos de Hig. Saúde Pública*. São Paulo. 1943 Sept. v 8, No 19 85-102 4 fig [10 refs.] English summary

In his determination of the dissolved oxygen content of water in which were breeding the author used Winkler's method, which he descri

at length. A table gives the results of the test in 22 natural breeding places. *A. albitalis*, *A. fessibai*, *A. strodei* and *A. noroestensis* were found breeding in waters of varying degrees of organic pollution in which the dissolved oxygen content varied from 2.5 to 6 per million. *A. lanei*, *A. argyritarsis*, *A. darlingi*, *A. parvus*, *A. lutzii* and *A. autumensis* showed a partiality for breeding in well oxygenated waters with much green vegetation. The dissolved oxygen in their breeding places varied from 6.5 to 9.5 parts per million.

In the laboratory water containing larvae of *A. albitalis*, *A. argyritarsis*, *A. strodei* and *A. noroestensis* was slowly disoxygenated. The larvae remained active as long as the oxygen content was above 4 parts per million. When it was reduced to 1.5 parts per million the larvae died.

The author concludes that the pollution with organic matter of breeding places of *Anopheles* of the *Nyssorhynchus* group is an efficient and economical anti-larval measure.

Norman White

LUTI O. Ferro dos criadouros de anófeles e o anofelismo sem malária do vale do Paraíba. [The Iron Content of Anopheline Breeding Waters in Malarial Regions and in the Malaria-free Paraíba Valley.] *Arquivos de Hig. e Saúde Pública* São Paulo 1943 Sept. 18 No. 19 105-17. English summary.

There was a popular belief that the freedom from malaria that the valley of the Paraíba River enjoys between Guararema and Quiluz in spite of the presence of anophelines was due to the high iron content of the water of that river. To test the foundations for such a belief the author carried out a large number of observations. The iron content of waters in which *Anopheles* were breeding was determined in many places. There was no significant difference between the iron contents of waters in malarious and malaria-free areas. In the Northern Seaboard where malaria is endemic the waters are excessively ferruginous much more so than the water of the Paraíba River.

Norman White

BOL. OFICINA SANITARIA PANAMERICANA 1944 June 13 No. 6 491-505. Segundo informe de la Comisión Panamericana de Malaria. [Second Report of the Pan-American Malaria Commission.]

This report contains a list of *Anopheles* known in North and South America and lists are given of the anopheline fauna found in each of the countries. In addition there is a brief account of the amount of anti-malaria work completed in the years 1941-43.

Charles H. Hicks

GUPTA R. D. & LAHA P. N. Hemiplegia in Chronic Malaria. *J. Indian Med. Ass.* 1944 July 13 No. 10 296.

An Indian boy, aged six years, was admitted to hospital with a history of fever for two months and on the previous day a sudden onset of paralysis of the arm and leg on the right side. On admission his temperature, pulse rate and respiration rate were normal; his face was pale and the spleen was enlarged to three inches below the ribs. Examination of the blood showed erythrocytes 3,350,000 per cmm, haemoglobin 60 per cent, no malarial parasites and negative W.R. The right arm and leg were completely paralysed and there was also slight facial paralysis on the right side; the tendon jerks were increased slightly; the superficial abdominal reflexes on the right side were absent; the plantar reflex on the right side was extensor; there was apparently no loss of sensation.

He was given quinine sulphate 3 grains thrice daily. The paralysis of the face and right arm disappeared by the third day and that of the leg by the fifth.

day and he could then walk about freely. The reflexes had also become normal by then. His temperature had been afebrile throughout his stay in hospital. He was discharged cured.

The authors think that the symptoms were caused by embolism of malarial parasites in the left internal capsule. [ECKSTERN this *Bulletin* 1943 v 40 517 mentions a somewhat similar case but tertian fever was present.]

J F Corson

LANCET 1944 Nov 18 667-8 BRIT MED J 1944 Nov 18 664
Mepacrine for Malaria. Statement by MRC Committee on Malaria.

In view of the great importance of malaria for warfare in the Far East and also in the Mediterranean region a great deal of work has been carried out during recent years to evaluate the relative merits of the two chief antimalarial drugs available at the present time—viz mepacrine (Atebrin Quinacrine) and quinine. The conclusions reached are shown by the resolutions (reproduced below) which have recently been adopted by the appropriate official bodies in the United States and in this country.

AN AMERICAN RESOLUTION

According to the *Journal of the American Medical Association* (1944 125 977) the Board for the Co-ordination of Malarial Studies adopted the following resolution concerning the relative value to the armed forces of mepacrine (quinacrine hydrochloride USP) quinine and totaquine (L SP).

"On the basis of controlled quantitative studies in civilian Army and Navy establishments the evidence at hand justifies the following statement:

1. *In the suppressive therapy*—Mepacrine (atabrine) has proved to have all the antimalarial properties ascribed to quinine in the suppression of malaria during and subsequent to exposure to infected mosquitoes. Effective suppression can be accomplished over long periods of time by proper use of mepacrine. Available evidence indicates that this end may be achieved without danger to the individual.

"Earlier reports indicated a significant incidence of gastro-intestinal disturbances in certain groups of men receiving suppressive mepacrine therapy. For practical purposes these adverse reactions can be avoided by proper administration of the drug. Quinine in doses adequate to assure suppression of malaria equivalent to that produced by mepacrine in the dosage currently used by the armed forces is frequently attended by symptoms of cinchonism.

Mepacrine has been demonstrated to prevent consistently the development of falciparum malaria when the drug is administered in proper dosage before during and after exposure.

2. *In the therapy of the acute attack*—Experience in the past two years has demonstrated conclusively that mepacrine (atabrine) when properly administered is fully as effective as quinine in the termination of the acute attack and is safer than quinine. The intramuscular injection of mepacrine is highly effective in securing a rapid therapeutic response. Evidence is not at hand to decide on the relative merits of mepacrine administered intramuscularly as compared with quinine administered intravenously in patients with fulminating cerebral malaria.

3. *In the therapy of vivax malaria*—Neither mepacrine nor quinine can be relied on to prevent relapses in vivax malaria following the discontinuation of therapy, although the interval between attacks is significantly longer following mepacrine than following quinine in the dosage schedules currently used by the armed forces.

4 *In the therapy of falciparum malaria*—There is convincing evidence that mepacrine not only suppresses the clinical symptoms of falciparum malaria but also cures this malignant form. The evidence of a similar curative effect of quinine is not conclusive.

5 *Totaquine (USP)*—Because of its content of crystallisable cinchona alkaloids totaquine (USP) has activity which approximates to that of quinine and therefore can be used as a substitute for quinine when given orally. The antimalarial activity of totaquine (USP) is dependent on the amount of crystallisable alkaloids in the preparation rather than on the specific amount of each individual alkaloid. Gastrointestinal disturbances occur more frequently following the use of the present totaquine (USP) than they do following the use of quinine or mepacrine.

On the basis of the foregoing statement it is resolved (1) that no advantage and possible disadvantage would accrue to the armed forces were quinine or totaquine to replace mepacrine for the routine suppression and treatment of malaria. (2) That the large scale production of quinine or totaquine is not now considered a matter of importance for the management of malaria among Army and Navy personnel. It is possible that a supply of totaquine in excess of the present stockpiles may be required for therapy in civilian populations temporarily under the jurisdiction of the armed forces in occupied territory where immediate dissemination of information concerning the use of mepacrine (atabrine) is not practicable. In this connexion it should be kept in mind that after the war the overall need for all established antimalarial drugs will continue to be great.

The personnel of the Board is R. F. Loeb (chairman), W. M. Clark, R. G. Coatney, L. T. Coggeshall, F. R. Dicuade, A. R. Dochez, E. G. Hakansson, E. K. Marshall jun., O. R. McCoy, F. T. Norris, W. H. Sebrell, J. A. Shannon and G. A. Carden jun. (secretary).

BRITISH CONCLUSIONS

The above resolution was considered by the Drug Prophylaxis and Therapy Subcommittees of the Medical Research Council Committee on Malaria at a joint meeting on August 23, 1944. The members of these subcommittees are Major-General A. G. Buggam (chairman), Brigadier F. A. E. Crew, F.R.S., Colonel S. P. James, F.R.S., Dr W. D. Nicol, Lieut.-Colonel B. G. Macgregair, Colonel C. S. Ryles, Mr P. G. Shute, Brigadier J. A. Sinton, F.R.S., Air Marshal Sir Harold Whittingham and Dr F. Hawking (secretary). The various items were discussed and it was agreed that British experience and the extensive investigations carried out in Australia under the direction of Brigadier N. Hamilton Fairley led to the same conclusions as those reached in America. In particular the subcommittees endorsed the resolution that if quinine or totaquine replaced mepacrine for the routine suppression and treatment of malaria, the change would not be advantageous and might possibly be disadvantageous.

It is not possible during war time to disclose all the extensive investigations upon which these official American and British resolutions concerning the relative merits of mepacrine and quinine have been based, but when peace returns full details will doubtless be published in the scientific press. Meanwhile the position may be summed up by saying under proper administration mepacrine is no more liable to cause serious toxic effects than quinine is. Mepacrine is as effective as quinine in the therapy of vivax malaria but neither compound will prevent relapses at a later date. Mepacrine if properly given will practically always suppress and cure falciparum malaria while the action of quinine in this respect is less certain.

Accordingly it must be realised that mepacrine is not an inferior substitute for quinine forced upon us by the loss of Java, but it is a more effective agent against malaria which would still be employed even if the supplies of quinine were unlimited.

ATKINSON M. E. & ECKERT H. W. The Photospectrometric Determination of Atrabine. *J Biol Chem* 1944 Aug v 154 No 3 597-603 [17 refs.]

The method described is a modification of that of MASTIX (*J Biol Chem* 1943 v 148 529) and BRODIE and LEVINE (*this Bulletin* 1944 v 41 433). The chief new point is the intensification of the fluorescence of mepacrine by means of caffeine sodium benzoate.

Technique for Blood—Pipette 5 ml. of oxalated whole blood into a 125-ml. Squibb separatory funnel containing 10 ml. of 5 per cent disodium phosphate solution. Add 30 ml. of ether and shake for three minutes. Very little emulsion forms. Allow the two layers to separate and tap off the aqueous layer. Wash the ether layer with three portions of about 5 ml. of 0.03 N sodium hydroxide and once with 5 ml. of distilled water.

To the ether layer add 5 ml. of 0.1 N sulphuric acid and shake for 30 seconds. Collect the acid extract in a 25-ml. glass-stoppered graduated cylinder. Extract the ether with a second 5-ml. portion of acid, adding the second extract to the first. Wash down the stopper with about 2 ml. of water, shake to collect as much as possible of the aqueous layer in the bottom of the funnel, and add this final wash to the collected acid extracts. Dilute to the 15 ml. mark with water. Add 1 ml. of the caffeine reagent, stopper and mix. The solution is then ready to read in the fluorometer. The standard for comparison consists of a mixture of 1 µl. of atrabine (1 ml. of diluted standard) with 10 ml. of 0.1 N H_2SO_4 and 1 ml. of caffeine reagent diluted to 16 ml. with water. Deduct from all readings the apparent fluorescence of a blank consisting of 10 ml. of 0.1 N H_2SO_4 plus 1 ml. of caffeine reagent diluted to 16 ml. with water.

The caffeine reagent is prepared by dissolving 10 gm. of caffeine sodium benzoate in 30 ml. water and 40 ml. 85 per cent ethanol, add 20 ml. of diethanolamine, dilute to 100 ml. with water and mix. The readings are made with a Coleman No. 12 photofluorimeter. 5 ml. samples of blood containing 1 microgramme of mepacrine can be analysed satisfactorily. If the room temperature is above 24°C the sensitivity is diminished.

[For many additional technical details the original should be consulted. Dr. E. J. KIRC, who has tried this method, states that difficulty may often be encountered owing to fluorescent substances present as contaminants in caffeine sodium benzoate and in diethanolamine.] F. Harding

LEVI O. Metodo simples e rápido para a dosagem do quínino no sangue. (Nota preliminar.) [A Simple and Rapid Method for the Estimation of Quinine in Blood. (Preliminary Note).] *Arquivos de Hig e Saúda Pública*, São Paulo 1943 Sept. v 8 No. 19 75-82. English summary.

One cubic centimetre of blood is dehydrated by mixture with 3 gm. desiccated sodium sulphate. It is triturated and transferred to a 25 cc. flask and four to five drops of ammonia are added to make it alkaline. The alkaloid is extracted with 8 cc. chloroform 80 per cent. ether 20 per cent. on a water bath at 65°C. The flask is cooled and the supernatant is decanted into another flask. This operation is repeated twice with 5 cc. quantities of the same mixture and then the combined supernatant fluids are evaporated to dryness. The residue is dissolved in 2 per cent. sulphuric acid in water and made up to the original volume of 1 cc. The concentration of quinine is estimated by comparing the

fluorescence obtained with that of known solutions of quinine sulphate. The sensitivity of the method depends upon the apparatus used to detect the fluorescence [and presumably upon the volume of blood originally taken]. The author could detect quinine in a concentration of 1 in 6 millions i.e. 0.17 micrograms per cc. of blood. When quinine in known amounts was added to blood, the loss in recovery was between 10 and 15 per cent. Quantities of blood as small as 0.2 cc. may be used. The time required for an assay is about 25 minutes. [Abstract prepared from English summary.] *F Hawking*

MCGREGOR I S & LOEWENSTEIN A Quinine Blindness. *Lancet* 1944 Oct 28 566-7

A most interesting case is described of a man aged 37 who had taken quinine over a period of years in small doses without any ill effects except tinnitus and transient deafness. About 360 grains were administered within a period of 24 hours. He became deaf and totally blind. Very slow and imperfect recovery took place and although at times the central vision was good his field of vision remained restricted. It was necessary for him to be rehabilitated as a person with grossly defective vision. The authors state that the man did not lose his eyesight because he had an idiosyncrasy; he lost it because he was given massive doses of quinine. To avoid such catastrophe quinine dosage should be cautious and the drug stopped if visual symptoms arise. [As this patient had deafness and tinnitus on previous occasions it would be wise to include attention to these symptoms in this important warning.] *W J B Riddell*

1 GOOD R II BLACKLOCK D B Arsenic in Malaria. [Correspondence.] *Brit Med J* 1944 Oct 28 579 and Nov 15 671

i In the author's experience a single intravenous injection of 0.45 gm. of neoarsphenamine always terminated artificially induced benign tertian malarial infection; he suggests that it might be tried in cases of naturally acquired malaria that do not respond to quinine etc.

ii BLACKLOCK refers to studies made from 1917 to 1920 by a team of workers at the Liverpool School of Tropical Medicine [this *Bulletin* v 11 to v 15]. These workers found [*ibid* 1919 v 13 79], that neoarsphenamine had a rapidly effective action on *Plasmodium vivax* infections but the ultimate results were most disappointing as nearly all cases relapsed; a combination of neoarsphenamine and quinine however [*ibid* 1920 v 15 121] was more effective than either drug alone. In infections with *P. falciparum* [*ibid* 1919 v 14 281] or *P. malariae* [*ibid* 1920 v 15 121] neoarsphenamine had no good effect. In one series of cases however [*ibid* 1919 v 13 289] the administration of Liq. Arsenicalis B P after two initial intramuscular injections of 15 grains of quinine bi by drochloride prevented relapses during the observation period of 60 days. Of 31 cases so treated only four (12.5 per cent.) relapsed while in 30 control cases treated with the two quinine injections only 21 (70 per cent.) relapsed. The cases treated had long-standing infections with frequent relapses in spite of much treatment with quinine. *J F Corson*

NEEMAN M. Configuration and Antiplasmodial Activity. [Correspondence.] *Nature* 1944 Oct 28 550

SLIWITSKY M. Beitrag zur Malariaabkämpfung im heutigen Bulgarien. [Control of Malaria in Bulgarian occupied Thrace and Macedonia. (*Dent Tropenmed Ztschr* 1943 Dec. 1 v 47 No 23/24 613-24 6 figs. [10 refs.]

The author reviews the researches of various workers on the races of *Anopheles maculipennis* in the Balkan Peninsula during the past twelve years or so most

of which have been recorded in this *Bulletin* [for example 1935 v 32, 101 1936 v 33 259 & 762 1937 v 34 166 1938 v 35 137 138]

From December 1941 to May 1942, an antimalaria campaign was carried on by a team of workers in Thrace and Macedonia, bordering on the Aegean Sea. The chief measures were the destruction of hibernating adult mosquitoes in houses and cattle sheds, destruction of mosquito larvae by oiling or by stocking the pools with *Gambusia* fish and treatment of malaria carriers. Adult mosquitoes were sought for with torches and sprayed with "Fly Tox". Malaria carriers were given a 10-day course of quino-plasmoquine, three tablets daily. The results were very satisfactory.

A case of blackwater fever occurred in March 1943 in a soldier who had had benign tertian fever in the previous summer. The patient recovered after treatment with "Campolon" [a liver extract] and "Cantan" [vitamin C] and diuretin [theobromine and sodium salicylate given in tea. (No mention is made of a blood examination in this case.)] J. F. Corson

STRUBERNY L. Die Malariaekämpfung und ihre Resultate im bulgarischen Heere in den Jahren 1942 und 1943. (*The Antimalaria Campaign in the Bulgarian Army*). *Deut. Tropenmed. Zeitschr.* 1943 Dec 1 v 47 No. 23/24 624-6

The chief cause of the great spread of malaria in the Bulgarian army was the heavy infection of the population of the newly acquired countries of Thrace and Macedonia. A study of the biological and epidemiological conditions formed the foundation for the application of control measures.

The general result of the antimalaria campaign in the army in 1941 was very good. From May 1st to October 31st the average incidence of malaria in the garrison troops was 18.21 per thousand, while in the previous year it was 45.8 per thousand. Among the mobilized troops and labour battalions in heavily infected areas of Thrace, and near the Turkish border the average incidence in 1941 was 94.77 per thousand and in 1942 it was 121.16 per thousand. This is much less than during the Great War of 1915-1918, when subtertian malaria was the chief form of the disease.

The usual measures were applied and are given in some detail. They included filling up or oiling breeding places, spraying dwelling rooms, the use of mosquito gauze, blood examinations, treatment of patients and malaria carriers and prophylactic administration of quinine (1-2 gm.) or (for airmen) atabrin (2 x 0.1 gm.) twice a week. The results were considered to be good. J. F. Corson

KHAN H. On the relative value of certain Larvivorous Fishes from the Punjab, with Notes on their Habits and Habitats. *Indian J. Vet. Sci. & Animal Husbandry* 1943, Dec. v 13 Pt. 4 315-25 [23 refs.]

GAJEWSKI J. E. & TATUM A. L. A Study of the Mechanism of Relapse in Avian Malaria. *J. Infect. Dis.* 1944 Mar-Apr v 74 No. 2, 85-92. [21 refs.]

It is well known that various factors conduce to relapse in malaria in which there is a return of fever together with the reappearance of parasites in the peripheral blood. Of the causes of relapse there are acute infections of other sorts, exposure to cold, exhaustion, anaesthesia, surgical changes in climate and removal from low to high altitudes. Spontaneous relapses have been noted in avian malaria and these may vary with the season or occur more frequently when barometric pressure is low. Relapses have been produced by the injection of parasitized or normal erythrocytes or foreign blood, or by ultra violet radiation, especially when resistance has been lowered by intercurrent infections.

It has recently been shown that the relapse following intravenous injection of foreign avian washed erythrocytes is associated with blockage of the reticulo-endothelial system by these erythrocytes. Injection of epinephrine may also bring about relapse. Sudden reduction of the number of erythrocytes or haemolysis following injections of phenylhydrazine is another cause. HEGNER and his co-workers [this *Bulletin* 1939 v 36 338] having shown that the merozoites of certain avian malarial parasites had a preference for young rather than old erythrocytes considered it possible that the severity of infections would vary with the proportion of young to old erythrocytes present in the blood during the developing infection. As it was known that exposure to an atmosphere rich in oxygen depressed red cell production while an atmosphere poor in oxygen stimulated it HEGNER and DOBLER (*Amer J Hyg* 1941 v 34 Sect. C 14) studied the infection in birds during exposure to an atmosphere with high oxygen content. As they predicted the reduction in the young erythrocytes was associated with infections of reduced severity. The converse condition was not studied by them. In the present paper the authors give an account of experiments in which the influence of an atmosphere of low oxygen content on latent infections in bird malaria was under observation.

It was found that an oxygen content of approximately 75 mm Hg partial pressure brought about relapse in two to seven days in all of more than 100 canaries with latent *P. cathemerium* infection. At the peak of the relapse the infection was less intense than at the peak of a primary attack. After two to four days the infection declined till at the end of a week parasites were no longer detectable. The mortality rate in the primary infections was about 30 per cent. After several weeks the birds were again exposed to the low oxygen atmosphere. This time only 50 per cent relapsed usually with slight infections. The exposure when repeated a third time caused no relapses while of 10 such birds two were found to be susceptible to re-inoculation with the same strain of parasite. It would appear that in these two birds a cure had been effected.

It was found that birds in which the primary attack had been cut short by administration of plasmoquine, atahrine or quinine relapsed earlier and more severely when exposed to the low oxygen atmosphere than did birds which had survived the primary infection without drug treatment. This was particularly noticeable in the case of birds which had received plasmoquine. It was evident that birds in which the infection had run its natural course had in some manner developed a greater resistance than the treated birds. It was also observed that if at the first exposure while the parasite count is rising the bird is removed from the low oxygen chamber the count falls promptly. On re-introduction to the chamber the count rises again. This procedure with like result was repeated four or five times. It seemed evident that the low oxygen in some way interfered with progress of phagocytosis.

From the work of the TALIAFERROS [this *Bulletin* 1930 v 27 288] and CANNON [*ibid* 1931 v 28 494] it was known that the injection of large numbers of infected erythrocytes into the blood stream of latent birds is followed by their rapid disappearance from the blood as a result of phagocytosis by the macrophages of the liver, spleen and bone marrow. These observations were confirmed by the authors of the paper under review. They also showed that an exposure of 16 hours to the low oxygen atmosphere brought about a condition of hyperglycaemia. If at this stage infected erythrocytes were injected intravenously there was not the rapid disappearance from the circulation as in latent birds not exposed to low oxygen. A similar failure to disappear occurred when hypodermic injections of epinephrine were made an hour before the infected erythrocytes were injected. As in the case of low oxygen exposure injection of epinephrine gives rise to a condition of hyperglycaemia. A similar

result was obtained when hyperglycaemia was produced by the hourly enteral administration of 0.5 cc. of 50 per cent. glucose solution.

In seeking for an explanation of these results the authors note that there is very little direct evidence of the presence of antibodies in malarial infection. There is no doubt, however, that some substance sensitizes the phagocytes to the extent that they remove the parasites from the peripheral blood. This substance is present in small amount only—just sufficient to keep the parasites at the low level characteristic of latency. It is postulated that under low oxygen tensions or as a result of hyperglycaemia the formation of the antibody is reduced to such a degree that the phagocytes are no longer capable of keeping the parasites at the low level. With continued low oxygen exposure this phase passes and parasites are again reduced. This could be interpreted as indicating a condition of hyperimmunity. Each relapse may be considered to be similar in action to injections of parasites which BOYD and KITCHEN (this *Bulletin* 1943 v 40 818) have shown produce an increase in immunity in patients who have had their primary attack of malaria. The instances noted above in which the infection was cut short by drug treatment may similarly be explained. It might be urged that exposure to an atmosphere with a high oxygen content should lead to an increased degree of immunity, but it is argued that such an increase in the oxygen does not bring about a corresponding saturation of the haemoglobin and depresses reticulocyte formation only to a slight extent. This study, however, is outside the scope of the paper.

C. M. Wenson

CALDWELL, F. E. In Vitro Effects of High Temperatures on Avian Malarial Parasites. *J. Infect. Dis.* 1944 May-June v 74 No. 3 189-205 2 figs. [Numerous refs.]

Apart from the observation of L. G. TALLAFERRO (*J. Prev. Med.* 1928 v 2, 515) that exposure of *Plasmodium californicum* to a temperature of 0.5°C *in vitro* resulted in a delay in the asexual development in proportion to the time of exposure, very little work has been done on the modifications in periodicity which can be produced by factors acting directly on the parasites. On the other hand many studies have been made on the modifications in the development of the parasites which result from changes in the environment or physiology of the host. To obtain further information on the effects of *in vitro* exposure it was decided to study strains of *P. californicum* which had resulted from exposure to sub-lethal temperatures. Working with the 3H1-2 strain it was first determined that it possessed a high degree of synchronism in asexual reproduction and had the ability to give rise to large numbers of gametocytes, as determined by its ability to produce oöcytes in *Culex pipiens*. Further experiments indicated that the thermal death point was reached by exposing infected blood in capillary tubes to a temperature of 50°C for eight minutes and that strains could be started in canaries inoculated with blood exposed to this temperature for seven minutes. Three such strains were studied. The first of these (3H1-3) revealed a marked disturbance in the synchronism of schizogony and gametocyte production, which persisted in a number of birds for three months. During a further series of passages over 6½ months the strain had regained its original characters. The second strain (3H1-4) after one passage showed disturbance in the synchronism of schizogony and a marked reduction in gametocyte production. A further 6½ to 7 months study revealed a persistence in the disturbance to asexual reproduction, while gametocyte production was reduced to such a level that attempts to infect *Culex pipiens* were unsuccessful. The third strain (3H1-5) did not at any time show departure from the characters of the original strain (3H1-2). In addition

to discussion of the main results of the experiments the paper gives a historical review of relevant literature and details of the technique employed and the methods adopted for estimating changes in the cycle of development of the parasite.

C. M. HENYON

REDMOND W. B. Mosquito Transfer of the Pigeon Strain of *Plasmodium relictum* *J Infect Dis* 1944 May-June v 74 No 3 184-8.

A strain of *Plasmodium relictum* discovered in a pigeon was inoculated to pigeons and canaries. The strain in canaries was re-inoculable to pigeons and there did not appear to be any appreciable differences between the parasites in the two hosts. Experiments described in this paper relate to attempts to transmit these infections by *Culex pipiens*. It was found that the infection was readily transmitted from canary to canary but was not transmitted from canary to pigeon nor from pigeon to pigeon. After passage of the strain from canary to canary through the mosquito 12 pigeons were inoculated intravenously. In only two of these were a few parasites seen. Later these birds contracted heavy infections when inoculated with the strain which had not been transmitted by *Culex pipiens*. Similar experiments with like results were carried out by injection of sporozoites dissected from infected mosquitoes. The author considers that the experiments indicate that passage through the mosquito has produced genetic alterations in the strain of parasites employed.

C. M. HENYON

BLACKWATER FEVER.

BENTLEY T. H. C. Blackwater Fever and Vascular Collapse. [Correspondence *Lancet* 1944 Nov 18 674-5]

This letter referring to the generalized vascular disturbance described in blackwater fever by MAEGRAITH and FINDLAY [see this *Bulletin* 1945 v 42 12] draws attention to the association of intravascular haemolysis and vascular dysfunction in conditions such as Raynaud's disease and paroxysmal cold haemoglobinuria where auto-antibodies have been found.

Some original experiments are described briefly in which intravenous injection into rabbits of a small amount of high titre cold agglutinating serum from a patient with Raynaud's disease proved lethal from anaphylactic shock with haemolysis and vascular spasm. Average [human] serum has no such effect on them. An attempt at prophylaxis by injecting suspensions of lecithin as an alternative antigen had a considerable degree of success.

The author suggests that some such measure might be useful clinically in these various conditions including blackwater fever although lecithin itself a lytic agent might not be appropriate.

E. G. L. BYRATERS

BLACKIE W. A. Blackwater Fever *Clin Proc Cape Town* 1944 July-Aug v 3 No 6 272-312. [36 refs.]

TRYPANOSOMIASIS.

VAN HOOF, L. HENRARD C. & PEEL, E. Morphologie des trypanosomes polymorphes des mammifères dans les glandes salivaires de *G. palpalis*. [Morphology of Polymorphic Mammalian Trypanosomes in the Salivary Glands of *G. palpalis*.] *Rec Travaux Sci Méd. Congo Belge* Léopoldville. 1944 Jan. No 2, 204-19 3 pls.

This paper deals with the vexed question regarding the differential diagnosis of the three polymorphic mammalian trypanosomes *Trypanosoma gambiense*, *T. rhodesiense* and *T. brucei*. Though so different in their host-parasite relationships and clinical manifestations the blood forms of these parasites are morphologically indistinguishable. It is true that at one time it was held that *T. rhodesiense* and *T. brucei* differed from *T. gambiense* in the presence of the "posterior-nuclear" forms in experimental infections of laboratory animals, but the finding of similar forms in unquestionable strains of *T. gambiense* (first demonstrated in East Africa and subsequently in West Africa) invalidated this criterion, since the difference between the two subgroups—*T. rhodesiense* with *T. brucei* on the one hand, and *T. gambiense* on the other—proved to be merely a quantitative and fluctuating character. From the purely zoological point of view therefore these three parasites could hardly be regarded as independent species but rather as biological races of a single species (see this *Bulletin* 1944 v 41 150).

The Belgian authors have turned to the stages of development of these trypanosomes in the salivary glands of the tsetse fly for a solution of this problem. In the course of transmission experiments with *Glossina palpalis* they have observed certain peculiarities in the salivary stages of development of the three polymorphic trypanosomes which can serve to differentiate infections with *T. gambiense* on the one hand from infections with trypanosomes of the *T. rhodesiense-brucei* subgroup on the other both in fresh and in stained preparations. Although all the stages of development in the salivary medium are identical in these three trypanosomes and therefore morphologically indistinguishable the infections can be readily differentiated by the distribution, relative numbers and dimensions of the various developmental forms.

The observations recorded in this paper were based on four strains of *T. brucei*, two of *T. rhodesiense* and more than 100 of *T. gambiense*. The differential characters of the two subgroups of trypanosomes as seen in the salivary medium, are given in the table below which has been compiled from the table adduced in the original paper and from data given in the text.

The fact that the salivary forms of *T. brucei* and *T. rhodesiense* are indistinguishable from each other but differ from those of *T. gambiense* is also used as an argument in support of the view that the first two species are more closely related and form a subgroup independent of *T. gambiense*. Incidentally the authors mention an experiment in which a volunteer was inoculated with one strain of *T. brucei* but failed to acquire an infection. The paper is illustrated by four plates of figures.

[Among the developmental forms described in this paper some like the vacuolated globular ones and those showing multiple division, would appear to be abnormal: such aberrant forms occur in various other trypanosomes both in the vertebrate and in the invertebrate hosts. Indeed, the authors themselves do not attach any other significance to them. However if certain atypical forms are more commonly found in some polymorphic trypanosomes than in others, their recognition is undoubtedly of diagnostic value. Nevertheless, since the differences between the two subgroups are purely relative the three species of polymorphic trypanosomes must still be regarded as morphologically identical.]

TABLE

	<i>T gambiense</i>	<i>T rhodesiense</i> and <i>T brucei</i>
In fresh preparation	Massive infection extending throughout the salivary gland. Trypanosomes grouped in bunches or tufts. Long and slender forms in the ducts. Free forms in the gland or in the lumen of the excretory duct these are rarely the long proventricular forms but usually short forms resembling the stumpy blood forms. Globular vacuolated forms are rare.	Infection not so dense sporadic, sometimes leaving long stretches of the salivary gland free. Trypanosomes more frequently isolated than grouped in bunches when assembled together they do not form tufts characteristic of <i>T gambiense</i> . The ducts usually contain small short motile forms in the lumen there are free short forms very rarely long forms. Globular vacuolated forms are more numerous and larger than in <i>T gambiense</i> .
In stained preparation	Bunches of trypanosomes and crithidial forms attached to each other by the posterior (astagellar) ends. Isolated trypanosomes and crithidial forms rarely vacuolated but, when present, the vacuole is small. Few rounded forms with large vacuole 1 or 2 nuclei and 1 or 2 flagella.	Protoplasmic masses of syncytial appearance with multiple nuclei and flagella. Isolated trypanosomes and crithidial forms, frequently vacuolated the vacuoles being large. Numerous rounded forms with very large vacuole sometimes with parallel filaments resembling mitotic spindle. (These are the most characteristic forms in the <i>brucei rhodesiense</i> subgroup)

It is stated that the salivary forms do not vary with the host from which the tsetse became infected and that in all strains of known origin the differential diagnosis of the polymorphic trypanosomes conforms to the scheme outlined above.

Furthermore though the authors insist on the infallibility of their method of differentiation, several facts mentioned in the paper appear to be contradictory. Thus (1) two out of three Tanganyika strains of *T brucei* used in DUKE's experiments (this *Bulletin* 1933 v 30 469) produced in tsetse flies massive infections of the salivary glands (2) the authors note that in two of their own strains of *T brucei* the proportion of sparse salivary infections was 46 and 54 per cent. respectively from which it is evident that in both cases almost half of the infections in the flies must have been heavy (3) the authors found that a Uganda strain of *T rhodesiense* had all the characteristics of *T gambiense* in the salivary glands of the tsetse. On account of this and because the strain in question occurred outside the endemic area of *T rhodesiense* the Belgian authors express some doubt regarding the identity of this strain. However if the strain in question is from case Okero described by DUKE (this *Bulletin* 1931 v 28 346)—as it appears to be—it would seem that it originally showed all the characteristic features of *T rhodesiense*.]

C A Hoare.

CHORLEY T W *Glossina palpalis fuscipes* Breeding away from Water (Diptera) *Proc Roy Entom. Soc of London* Ser A. General Entom. 1944 Mar 23 v 19 Pts. 1-3 1-4

It appears that there are no clear records of *Glossina palpalis* breeding more than a mile from water. If conditions of vegetation and climate are suitable the author finds that it may breed many miles from water.

In Busoga, Uganda, there are areas of dense humid forest, broken up by elephant tracks which provide small openings and mixed light and shade suitable to this fly. In this at distances up to 12 miles from water one may find considerable numbers of adults and pupae of *Glossina palpalis fuscipes*. In the author's view the general limitation of this insect to waterside forest is not due to the presence of animals which serve as food supply (and which are often common in areas far from water uninhabited by this fly) but to climatic conditions of which he names shade and humidity. P A Buxton

POTTS W H Tsetse Hybrids. Correspondence *Nature* 1944 Nov 11 608-7

In 1836 the author crossed various species of *Glossina* with the idea that if the hybrids were sterile the method might be tried as a measure of control. As the females were not bred from isolated single pupae the possibility of fertilization of the newly hatched females by newly hatched males of the same species could not be excluded and the results were therefore not published [a brief mention is made by the author in *Bull Entom Res.* 1937 v 38 135]. Since then hybrids following the mating of *G morsitans* with *G swynnertoni* have been obtained by VANDERPLANK [below] and a recent examination of the male "hybrids" of the author's earlier experiments has shown that they differ from both parents. An account of those experiments is therefore now given.

Three out of 23 female *G swynnertoni* paired with *G morsitans* and surviving for 21 days or more, produced one, two and four pupae respectively, and from these two male and two female flies emerged, and a fifth fly escaped before its sex was known. They all resembled the female parent. Three out of 40 female *G morsitans* paired with *G swynnertoni* produced two, one and two pupae, respectively, and two males and three female flies emerged. These all resembled the male parent so they must have been hybrids. The external characters of *G swynnertoni* are dominant. The author calls the former hybrids (*G morsitans* father) "moratoni" and the latter (*G swynnertoni* father) "swynnertani". The following further crossings were made —

1 "moratoni" female	x <i>G swynnertoni</i>	4 pupae.
1 "moratoni" female	x <i>G morsitans</i>	4 "
2 "swynnertani" female	x <i>G swynnertoni</i>	5 " (3 and 2).
1 "swynnertani" female	x "moratoni"	0 "

From these 13 pupae seven imagines emerged—five females and one male (one escaped). One female was crossed with *G swynnertoni*; one with *G morsitans*; two with "moratoni" and one with the single male hybrid of the second generation: none produced offspring. As a control of the laboratory conditions each species was still breeding, between sexes of the same species after four generations.

As cross-mating seemed to occur less readily than mating within the species, and as the hybrids were so few the experiment was abandoned as not fulfilling the conditions necessary for control of the fly in the field. Recent experiments by Vanderplank [below] have led to a further consideration of the subject, and it is proposed to attempt to control *Glossina* by introducing large numbers of pupae of the alien species into country where the indigenous species is not

plentiful the indigenous species might be exterminated by sterility and the introduced species might die out owing to unsuitable environment

Experiments to cross *G morsitans* and *G swynnertoni* with *G pallidipes*, *G palpalis* and *G austeni* had negative results but the numbers of flies used were small [STUHLMANN (S S Bulletin 1908 v 1 93) claimed to have observed parthenogenesis in tsetse flies twice KLEINE (ibid 1909 452) failed to obtain offspring by crossing *G palpalis* and *G morsitans* (his '*G morsitans*' were probably *G swynnertoni* from pupae from Ikoma) see also CORSON this Bulletin 1932 v 29 837] J F Corson

VANDERPLANK F L. Hybridization between Glossina Species and suggested New Method for Control of certain Species of Tsetse [Correspondence] Nature 1944 Nov 11 607-8

The author crossed *G morsitans* and *G swynnertoni* each species being bred from pupae obtained in an area from which the other species was absent. The flies were hatched from pupae kept singly in tubes or were isolated immediately on emergence from collections of pupae. The results are shown in the table —

Nature of cross	Females inseminated per cent.	Inseminated females living over 21 days which produced pupae per cent.	No. of pupae per inseminated female living over 21 days	Average life of females days
<i>G morsitans</i> ♂♂ × <i>G swynnertoni</i> ♀♀ (experiment)	92 (37)	10 (31)	0.1 (3)	70 (40)
<i>G swynnertoni</i> ♂♂ × <i>G swynnertoni</i> ♀♀ (control)	80 (12)	100 (7)	2.4 (17)	61 (12)
<i>G swynnertoni</i> ♂♂ × <i>G morsitans</i> ♀♀ (experiment)	96 (45)	24 (33)	0.4 (13)	68 (47)
<i>G morsitans</i> ♂♂ × <i>G morsitans</i> ♀♀ (control)	76 (19)	100 (10)	4.0 (40)	75 (9)

N.B.—The numbers in brackets give the totals on which the percentages or averages are based these are not the same throughout the table, as some females counted as inseminated on the evidence of dissection did not live long enough to produce pupae, and also some of the females which were used to give the average life were not dissected to show insemination.

Insemination occurred as readily in the cross matings as with the same species where no choice was offered but the cross matings produced far fewer pupae.

In other experiments it was found that *G pallidipes* did not readily mate with *G morsitans* and *G swynnertoni* no successful mating took place between female *G pallidipes* and other species one male *G pallidipes* mated with but did not inseminate one *G morsitans* and four male *G pallidipes* inseminated four *G swynnertoni* but there were no offspring. When equal numbers of male and female *G swynnertoni*, *G morsitans* and *G pallidipes* were mixed in a cage

30×30×30 cm. mating between *G. saynnerioni* and *G. morrisoni* occurred as readily as between the sexes of the same species and took place at random but there were no cross matings with *G. pallidipes*.

The male hybrids have distinct genitalia and show affinities to the female parent all the hybrids were similar to *G. saynnerioni* in external markings. Male hybrids inseminate females, both hybrids and non-hybrids but there has been no offspring. Attempts to cross female hybrids with pure bred males of both species have failed. The average length of life of the hybrid females was 106 days—longer than that of their female parents. A few hours after a female is inseminated it is no longer attractive to males and will not permit further coitus.

A field experiment of releasing large numbers of *G. morrisoni* in an isolated block of *G. saynnerioni* country has been begun.

The author hopes to publish further details of this work later. J. F. Corson.

MARUAK Dorothy N. Effect of X Irradiation of Rats upon their Resistance to *Trypanosoma lewini*. *J. Parasitology* 1944 Aug., v 30 No. 4 209-23, 9 figs. [38 refs.]

LEISHMANIASIS

SHUKLA H. E. Résumé of Recent Research on Kala-Azar with special reference to Assam. *Proc. Ann. General Meeting of Assam & Northern Bengal Branch Brit. Med. Ass. Shillong 4th-7th November 1943* 30-39 1944. Calcutta: Indian Tea Association.

This article though containing no new material, is a very interesting one from the historical point of view. It gives a brief account of kala azar in Assam and then passes on to a review of the various investigations which have been carried out there and which led, in the first place, to the discovery of the nature of the mysterious disease, and finally to the establishment of the fact that the sandfly *Phlebotomus argentipes* is the vector. The names of all those who took part in the investigations which extended over many years, are mentioned and, coming from one who himself played a prominent rôle in the researches, the article may be accepted as historically accurate. It will be a most useful guide to all those who wish to follow the course of the laborious work, which has only recently been crowned with success by the transmission of kala azar to five out of five volunteers by sandflies which had been infected by feeding on cases of the disease.

C. A. Wrayson

FERRI-LUZZI, G. Studio sul kala-azar in Eritrea. [Kala Azar in Eritrea.] *Boll. Soc. Ital. di Med. e Ig. Trop. (Sex. Eritrea)* 1943 v 2 No. 3 5-13. English summary.

The author describes 9 cases of kala-azar in adults (of whom 6 were Europeans living in Eritrea).

This disease seems to be endemic in the two lowlands and clinically is very similar to that known in Europe and elsewhere.

HOU P. C. An Investigation of Kala-Azar and Sand-Fly Incidence in an Endemic Kala-Azar Area in the Western Part of Szechuan. *Chinese Med. J.* 1943, Oct.-Dec., v 61 No. 4, 279-80.

CLOW J M Kala-Azar in Shensi Province *Chinese Med J* 1943 Oct.-Dec.
v 61 No 4 281-90

In a preliminary note published in 1941 [this *Bulletin* 1941 v 38 569] it was reported that kala azar was occurring in the province of Shensi. It was later noted that a case of the canine disease had also been observed. In the present paper 535 cases which have come under the author's supervision during 1940 and 1941 in Shensi are considered. Geographically Shensi is similar to the great plain of N China, where kala azar is prevalent in the provinces of Hopei Honan Shantung and Kiangsu. The habits of the natives are similar to those in N China and sandflies abound in the months of May and June. In Shensi kala-azar occurred sporadically but it now has become almost epidemic and constitutes a serious problem. Of the 535 patients seen in Shensi 514 apparently contracted their infection in the Central Shensi area many of them in and around Sian city. Some of the patients mostly adults came from neighbouring provinces. The disease which is most frequently seen in children and young adults conforms to the well-known classical descriptions. Diagnosis according to the author is best accomplished by sternal puncture. The chief complications were noma necrosis of the upper and lower jaw dysentery pneumoma and acute granulocytopenia. For treatment various drugs were employed as follows—neostam (231 cases) neostibosan (35 cases) urea stibamine (12 cases) stilbamidine (a few cases). Of these drugs the last in the small series treated gave the most rapid response though severe shock like symptoms of a transitory character were not uncommon after the injections. Urea stibamine appeared to be more curative but more toxic than neostibosan which was the least toxic of the drugs employed. Neostam occupied an intermediate position. Three gm. per 100 lb of body weight is the total quantity of neostam recommended but larger doses may be necessary especially in children. Some patients who were cured received over 8 gm without ill effect. Of 400 patients in whom treatment was completed 15 per cent were cured 16.5 per cent doubtfully cured 52.2 per cent improved and 16.3 per cent relapsed were moribund or died.

C M Wenyon

SARROUY C & GILLOT F Traitement rapide de la leishmaniose viscérale infantile par un nouveau dérivé stibé. [Rapid Treatment of Infantile Kala Azar with a New Antimony Derivative.] *Arch Inst Pasteur d'Algérie* 1943 Mar v 21 No 1 28-37 6 charts.

The authors report the successful treatment of nine cases of infantile kala azar in Algeria by means of the methyl-glucamine salt of para-amino-phenyl stibonic acid named pentastib. This compound has already been employed in veterinary practice and for the treatment of a few cases of kala azar [this *Bulletin* 1944 v 41 109] in which it was administered intravenously. The authors of the present paper have found that the intramuscular injection of the drug in relatively large doses daily for a few days is followed by immediate response as evidenced by the rapid fall in temperature the disappearance of the parasites and the improvement in the condition of the blood. The best results were obtained when the quantity of the drug to be administered was spread over the minimum number of days. Thus it is recommended that for each kilogramme of body weight 0.07 gm. of the drug should be injected daily for four days or 0.1 gm. daily for three days. Though in some cases the injections were followed by nausea or vomiting the reactions were much less frequent than when the drug was administered intravenously.

C M Wenyon

- SARROUT J DENDALE R. COMBE P., ARNAUD R. & GILLOT F. A Rapid Cure for Infantile Visceral Leishmaniasis by a New French Antimonial Derivative. *Texas Reports on Biol & Med* 1944 v 2, No 3 325-34 6 figs. [12 refs.]

This is an account of the same work as that noticed above.

- KIKUTHI W. Epidemiologie Uebertragung und Therapie der Leishmaniasis interna. [Epidemiology Transmission and Treatment of Kala Azar] *Wösch. med. Wösch.* 1943 Feb 5 104-8.

A general account.

- BERBERIAN D. A. Cutaneous Leishmaniasis (Oriental Sore). I. Time required for Development of Immunity after Vaccination. *Arch. Dermat. & Syph.* 1944 June v 49 No. 6 433-5.

The artificial production of oriental sore at selected sites by inoculation of leishmania from another sore or of cultures of leishmania, is now a recognized procedure in order to avoid the disfiguring sores which in natural infections, appear on exposed parts of the body particularly the face. Such artificially produced sores run a normal course and as in the naturally acquired disease are followed by complete immunity. The question arises how soon after the appearance of the sore is this immunity developed. Other observers have shown that during the development of one sore inoculation of infective material may be followed by another at the site of the second inoculation. To obtain further information on this subject the author produced oriental sore in a number of volunteers and at varying intervals after the appearance of the sore inoculated them a second time. In a series of experiments when the duration of the first sore had been 123 136 195 and 230 days a second inoculation produced a second sore, proving that immunity had not been developed. When the first sores had lasted 242 and 300 days, the second inoculation produced no sores. It seems clear that till the developing papule ulcerates and commences to heal and the leishmania disappear naturally from the lesion there is no immunity. This immunity is developed slowly and an individual inoculated for protective purposes is liable to acquire oriental sore naturally at any time during the long period required for development of this immunity. C. M. HENSON

FEVERS OF THE TYPHUS GROUP

- STEPHENSON C. S. Epidemic Typhus Fever and other Rickettsial Diseases of Military Importance. *New England J. of Med.* 1944, Sept. 21 v 231, No. 12, 407-13. [16 refs.]

- CIMINO V. Studio sull'andamento della febbre ricorrente e del dermatite in Asmara nel quadriennio 1939-1942. [Typhus and Relapsing Fever in Asmara, 1939-42.] *Boll. Soc. Ital. di Med. e Ig. Trop.* (Sez. Eritrea) 1943 v 2 No. 3 85-83 English summary

"Typhus and relapsing fever are two endemic diseases in Asmara that show epidemic recrudescence during the cold and rainy months of the year.

The European population is frequently affected, but with less intensity than the natives.

The epidemic period of typhus and relapsing fever are generally coincident

MACCHIAVELLO A. El tifo exantemático en el Ecuador. I. Estudio experimental de cepas aisladas en el Ecuador Interandino [Exanthematic Typhus in Ecuador. I. Experimental Study of Isolated Strains] *Rev. Facul. de Med. Bogotá* 1944 June v. 12 No. 12 694-709 [16 refs.] English summary

The author whose name is familiar in connexion with his method of staining describes the first detailed investigation of typhus rickettsiae in Ecuador. The first strain examined was isolated in Quito by another observer who passed it through guinea-pigs during the first three passages it behaved as a typical non-orchitic strain but on the fourth passage it appeared to become strongly orchitic and so was regarded as murine. At the fifth passage it was submitted to the author who found that the orchitis was caused by an inter-current infection with *Salmonella typhi murium*. Rickettsiae were still present in the vaginal scrapings but rats were found to be insusceptible to infection and so the strain was regarded as being of the classical type.

In the course of 17 passages in which 90 guinea-pigs were used only 14 of the animals showed typical febrile curves and in 11 of these rickettsiae were found in vaginal smears. Of the other guinea-pigs 32 died spontaneously and eight were used for immunity tests. None of the 14 with characteristic fever curves had scrotal reactions and rickettsiae were found in very small numbers when they were present.

By using brain substance as the inoculating material and by treating the animals with sulphathiazole a typical non-orchitic strain was gradually isolated.

The author holds that there is no justification for regarding the terms orchitic and murine as synonymous: some murine strains are orchitic others are not. On the other hand he believes that it is quite justifiable to call classical strains non-orchitic because even if some of these have originated from a murine strain they are in process of losing their orchitic properties through adaptation to the louse-man louse mode of transmission.

Two strains sent by Prof. Patiño-Camargo from Colombia were also investigated. One of these originated from suspensions derived from lice found on a typhus patient. In the course of 14 passages through 48 guinea-pigs it was found that very few of the animals gave typical febrile responses: most of them had slight irregular attacks or completely inapparent forms of the infection though even in animals suffering from inapparent attacks rickettsiae could often be found in small numbers in vaginal smears and the animals were found to have acquired immunity against other strains of typhus rickettsiae. During the later passages when the laboratory temperature was lower febrile reactions became more frequent. The second Colombian strain originated from the blood of a patient. This had been found by Prof. Patiño-Camargo to cause a scrotal reaction in 75 per cent of the male guinea-pigs through which passages were made. The author carried out 18 passages of this strain using 50 guinea-pigs and none of the animals showed the slightest degree of scrotal reaction. When brain substance was used as the inoculating material the strain died out after five passages but with tunica scrapings it was maintained. Its virulence was of the same low order as that of the other strain and its failure to cause orchitis could not be explained.

The author however suggests that the virulence of rickettsiae both in guinea-pig passages and in human infections may be influenced by temperature conditions and that these may prove to be important factors in connexion with the epidemiology of typhus fever.

John W. D. Megaw

GIROUD P & PANTHIER R. Au sujet du comportement du cobaye à l'inoculation péritonéale de virus typhique historique (The Response of the Guinea-pig to Peritoneal Inoculation with the Virus of Historic Typhus.) *Ann Inst Pasteur* 1944 May-June v 70 No 5-6 191-2.

GIROUD had already shown [this *Bulletin* 1938 v 33 926] that the historic virus could cause an orchitic reaction in guinea-pigs kept on a deficiency diet but the orchitic property of the strain could not be maintained in a definite manner. GIROUD and PANTHIER had also shown [this *Bulletin* 1943 v 40 35] that when massive doses of historic virus were obtained by rabbit-lung passage (starting from a blood-clot suspension from a patient suffering from louse typhus) inoculated guinea-pigs developed perorchitis with abundant rickettsiae in the exudate.

The present investigations deal with two strains the Nicolle-Tunis-Rabat strain and one of recent origin from a patient who contracted a severe infection in North Africa.

The Nicolle strain caused a scrotal reaction in guinea-pigs when rabbit-lung suspensions were injected intraperitoneally but behaved as a non-orchitic strain when brain and spleen suspensions were injected. Suspensions of spleen substance mixed with vaginal exudate caused orchitis up to the eighth guinea-pig passage, but the rickettsiae gradually became less numerous.

The other strain of recent human origin, behaved in much the same way, when passages were made with vaginal and spleen material the orchitic property was maintained and rickettsiae were found in vaginal smears up to the fifth passage. This strain was known to be of the true epidemic type because it was not pathogenic to rats.

The authors maintain that the same strain of historic rickettsiae can behave either as a typically orchitic or as a typically non-orchitic strain according to the conditions in which it is maintained and passaged. The guinea-pigs used in the present experiments were of the European type of variable weight and poorly nourished the authors' previous work was done with heavy well-fed, agoutis (*Dasyprocta* sp.)

JOHN W. D. MEGAW

BEGG A. M., FULTON F. & VAN DEN ENDE M. Inclusion Bodies in association with Typhus Rickettsiae. *J. Path. & Bact.* 1944 Jan. v 58 No 1 100-13 13 figs. (10 coloured) on 3 pls

With reference to the abstract of this paper in this *Bulletin* 1944 v 41 p. 838, the authors have requested the Bureau to explain that the coloured illustrations referred to in the abstract were microphotographs taken by the three-colour process and not coloured drawings. This point is not specifically mentioned in the legends to the coloured illustrations.

ASCHENBRENNER, R. Die Herz und Kreislaufstörungen beim Fleckfieber und ihre Behandlung (The Cardiac and Circulatory Disturbances in Typhus Fever and their Treatment.) *Klin. Woch.* 1943 Jan. 2 v 22 No. 1 1-8 7 figs. [36 refs.]

There were 106 deaths in the 691 cases of typhus fever treated by the author in 1942. The chief cause of death was damage to the central nervous system (90 cases) this was accompanied by pneumonia in 21 cases and by myocarditis in three. Altogether evidence of myocardial damage of a severe type was remarkably infrequent either by electrocardiographic examination during life or by post-mortem investigation and the author regards the condition as being of secondary importance. In his view mechanical and toxic damage to the vessels of the central nervous system plays a predominant part in the pathology

of the disease. There were three deaths from arterial thrombosis two from empyema and one each from septic oedema of the throat and myocarditis without severe cerebral symptoms

Various forms of treatment are discussed but the only drug that is referred to with special approval is strophanthin which was given in large doses daily during the febrile stage and in smaller doses in convalescence when evidence of circulatory disturbance persists

Sulphapyridine seemed to do harm rather than good even in cases with pneumonia.

John W D Megaw

ASCHENBRENNER R & MARX R Zur Frage des Nachfiebers in der Fleckfieber Rekonvaleszenz [The "After-Fever" in Convalescence from Typhus Fever] *Klin Woch* 1943 Feb 20 & 22 No. 8 159-62 3 figs [11 refs]

An unexplained rise of temperature was sometimes observed about the end of the first week of convalescence from typhus fever This lasts only one to three days in most cases and is of importance only because it is likely to cause needless anxiety The author suggests that it may be a late immunity reaction (See also this *Bulletin* 1942 & 39 542 1944 & 41 556 The paper contains a table showing the complications and sequelae observed in 691 cases of which 106 were fatal Apart from rashes these were —Bronchitis (348) pneumonia (83) after fever (46) diarrhoea (35) otitis media (34) septic throat (34) furunculosis (21) abscesses (10) empyema (9) parotitis (6) venous thrombosis (6) arterial thrombosis (4) and skin necrosis (4)

John W D Megaw

HIEDEK H KASPERCZIK K & FANTA H Kreislaufstörungen in der Fleckfiebergenesungszeit [Circulatory Disturbances in Convalescence from Typhus Fever] *Klin Woch* 1943 Feb 27 & 22 No 9 179-82 2 figs [15 refs]

This paper consists largely of a discussion of the relationship existing between the cardio-vascular and nervous disturbances occurring in typhus fever especially in the convalescent stage

Various disturbances of nervous origin are said to occur in 35 per cent of convalescent patients but cardio-vascular disorders are even more frequent and were observed in 45 per cent. of 500 patients studied by the authors Tachycardia was common even in patients who were resting cardiac pain and oppression were also prominent features in many cases. The pain was more uniformly associated with Head & zone in these cases than in angina pectoris. Numerous electrocardiograms were studied these showed that lesions of the heart played a secondary part in causing the cardiac disturbances which were regarded as being associated with damage to the vasomotor nerve centres and peripheral vessels The systolic blood pressure in the radial artery was higher than 130 mm in 31 per cent of 360 patients in whom it was tested during convalescence A curious feature was that although the radial systolic pressure showed the normal degree of increase on exertion the cerebral pressure (estimated by observations made on the retinal arteries) remained almost the same. By the tilt test it was found that when the body was placed in the head-down position at an angle of 45 degrees the systolic pressure in the cerebral arteries was usually increased much more than in normal persons. These observations and other evidence were regarded as pointing to lesions of the carotid sinus or of the vasomotor nerve centres. The beneficial effect of sympatol was considered to be evidence in support of this view

John W D Megaw

CROMO V Studio E. K. Grafico sul danno miocardico del dermatifo. 'Electrocardiography in Typhus.' *Boll. Soc. Ital. di Med. e Ig. Trop.* (Sez. Entrea) 1943 v 2, No. 4 23-43. English summary

Electrocardiography proves that during the course of typhus myocardial lesions more or less grave, are noted. Such lesions not only persist up to the 10th day of convalescence but very often get worse.

ROHMERS H Das Elektrokardiogramm in der Flecktyphus-Rekonvaleszenz. 'The Electrocardiogram in Convalescents from Typhus.' *Münch. Woch.* 1943, Mar 20 v 22, No 12, 234-6 12 refs

RAVEN R. W The Surgical Complications of Typhus Fever. *J. Roy. Army Med Corps* 1944 Sept v 83 No 3 119-22. 10 refs.

This brief account of the surgical complications of typhus fever is based on "many conversations with surgeons and physicians practising in North Africa and a study of the relevant literature." It deals chiefly with the infective complications most of which are caused by pyogenic organisms. DANIELOPOLU [this *Bulletin* 1918 v 11 131] is quoted as stating that streptococci are the commonest organisms and CONSTANTINE [*Algérie Med* 1941 207] as attributing 60 per cent of the complications to staphylococci and only 12.5 per cent. to streptococci.

The importance of early diagnosis and of resistance-building treatment is stressed. It might have been added that generous diet and good nursing will do much to reduce the incidence of these complications.

In a paper of three pages it is obviously impossible to give a complete account of the subject—for example the treatment of gangrene of the limbs is stated to consist in amputation well above the line of demarcation and no reference is made to the important matter of deciding when to amputate.

It is stated that there appears to be a racial resistance to the disease and an unnamed authority is quoted as saying that "the Rumanians have a high resistance, the French moderate and the Roumanians a low resistance supplicative complications always occurring." In view of the pronounced influence of age and environmental factors it is very doubtful whether inherited resistance plays any important part except perhaps in weeding out persons with low resisting powers. In the Rumanian epidemic so graphically described by Danielopolu environmental factors connected with war fully accounted for the low resisting powers of the people.

John W. D. Megar

HOYER v LORENSTERN M Ueber die günstige Wirkung durch Uebertragung von Rekonvaleszentenblut beim Flecktyphus. 'Favourable Effect of Convalescent Blood in Typhus.' *Münch. med. Woch.* 1943 Feb. 12, v 80 No. 7 119-20

ANDERSON C. R. Survival of *Rickettsia prowazeki* in Different Diluents. *J. Bacteriology* 1944 June v 47 No 6 519-22.

Rickettsia prowazeki suspended in sterile skim milk was found to survive up to 48 hours—in all the other fluids that were tested the survival time was much shorter. In distilled water or saline the viability of the organisms was almost completely lost after six hours and the addition of 1.0 per cent. glutathione made no difference. Broth with 20 per cent. normal yolk-sac fluid, and chick juice obtained in a cell-free condition from 8- to 10-day embryos, were favourable media but not so good as skim milk.

The survival time was estimated by inoculating groups of four cotton rats by the intracardiac route with standard doses of the various suspensions which were kept at laboratory temperature after preparation.

In another set of experiments suspensions of the livers of infected cotton rats were made in broth and then titrated at 0°C in saline broth and skim milk in ten fold dilutions. Within an hour of preparation the various dilutions were injected intraperitoneally into cotton rats and three weeks later the animals were tested for immunity.

Animals inoculated with dilutions made in skim milk or broth were found to have been protected by doses only 1-1 000 of those needed when the dilutions were made in saline.

Full details are given of the technique employed John H. D. Megaw

BERKOWITZ A. P. Notes on the Use of Duck and Turkey Eggs for the Large-Scale Preparation of Epidemic Typhus Vaccine. *South African J Med Sci* 1944 Aug v 9 No 3 109-10

The author found that the yield of anti typhus vaccine from each duck's egg was about five times greater than from a hen's egg. The great richness of the growth rendered processing of the vaccine much simpler.

Turkey's eggs gave yields equal to those of ducks' eggs.

The conditions of incubation are described John H. D. Megaw

HORRENBARGER R. & RENOUX G. Utilisation du mouton pour la preparation du vaccin antityphique (antirickettsien) non vivant d'après la méthode du Durand et Giroud. [The Use of Sheep in the Preparation of Typhus Vaccine.] *Arch Inst Pasteur d'Algérie* 1943 Mar v 21 No 1 4

The authors have obtained with sheep almost as good results as with rabbits in the multiplication of rickettsiae from which killed vaccine may be prepared. The animals are infected via the respiratory tract. The great advantage of sheep is that very large quantities of vaccine can be prepared and that the animals can easily be got and maintained.

Charles H. Steeds

DURAND P. BEGUET M. HORRENBARGER R. & RENOUX G. Recherche du pouvoir neutralisant du sérum des vaccinés contre le typhus exanthématique. [The Neutralizing Power of the Serum of Persons Vaccinated against Typhus.] *Arch Inst Pasteur d'Algérie* 1943 Mar v 21 No 1 1-3

Four groups of persons (in North Africa) were vaccinated with four vaccines of dead rickettsiae (formolized vaccine from mice and from rabbits [three doses] vanthate vaccine [three doses] and the same [two doses]). Three other groups were vaccinated with live vaccine (Blanc vaccine one dose. Laigret vaccine in two doses or by scarification). Serum was taken before vaccination and again three weeks after the last inoculation and was mixed undiluted or diluted 1/2 or 1/4 with 1/4 000 suspensions of infected mouse lung: the mixture was injected intradermally into a rabbit. Serum from 22 persons taken before vaccination neutralized the infective material and serum from 141 failed to do so. After vaccination the serum from 90 of the latter neutralized the lung suspension but whereas about 8/10 of those vaccinated with killed vaccines gave protective sera, only about 4/10 of those vaccinated with live vaccines did so. It seems therefore that killed vaccine is more effective than live vaccine in this respect.

[It seems unlikely that this test gives a clear-cut decision as to the presence or complete absence of neutralizing power and the fact that 22 sera neutralized the infective suspension before vaccination would lead to the suspicion that in some of the sera which failed to neutralize the infecting dose there might have

duration of the fever was 11 to 19 days a few cases lasted longer even up to 26 days in two instances. The pulse rate was relatively slow during the first week. In several patients the blood pressure fell to 100/80 by the 14th day. Evidence of cardiac weakness was common in the convalescent stage. The total leucocyte count was usually 9 000 to 12,000 per cmm. in two cases there was leucopenia.

A rash was observed in 17 out of 28 patients who were admitted early it appeared, on the fourth, fifth, or sixth day as dull red macules on the sides of the chest and soon spread over the trunk and limbs by the 12th day only brown staining persisted. No petechial haemorrhages were seen.

The face was flushed at the onset later it became bloated, and with swollen eyelids and reddened conjunctivae the patient had a drunken expression. Headache chiefly retro-orbital was early and intense in 45 patients. Backache and body pains occurred in 31 cases. Drowsiness and prostration occurred in all the patients. A special feature was the disappearance of the abdominal reflexes during the first week in every case. Coarse tremors of the limbs were present in convalescence in six patients depression at this stage was common. The spleen was palpable in four cases. Sore throat occurred, early in 15 cases, and later in five. Epigastric discomfort or pain occurred at an early stage in 28 cases. A dry cough was an almost universal feature during the second week in 25 cases it started early.

A local sore accompanied by lymphadenitis (which used to be regarded as of universal occurrence in mite typhus) was observed in only three patients. Convalescence was slow an average period of the two months rest was needed after the end of the fever and even then only light duty was permissible.

In 14 cases the end titres of the agglutination reactions were tested. *Proteus* OX19 was not agglutinated except for one reaction of 1-80. *Proteus* OAX titres ranged from 1-640 to 1-20 000 and in the whole series the maximum OAX titre was never less than 1-320 in any case. This reaction was the final diagnostic criterion. The rash often failed to appear even in white-skinned patients and it is stated that in a group of nine Indians admitted later for the disease, the rash was absent in all.

The treatment was on the lines suitable for louse borne typhus. Lumbar puncture was carried out in six cases for the relief of severe headache, and was effective in five of these. Dehydration resulting from difficulty in swallowing, pronounced in three subjects in two of these the Murphy drip was ceaseful, in the third intravenous saline with glucose was needed. Sulpha pyridine (5-8 gm. daily for five days) was given to 12 patients no benefit was observed and some of the patients suffered from unpleasant effects. Convalescent serum in doses of 15 cc. intravenously together with 14 cc. intramuscularly was given during the first week to two patients without obvious benefit.

Larval mites conforming in appearance to *Trombicula deliensis* were found on the dried leaves of palms and grasses in the affected area they were also found on rats of which the most numerous were *Rattus rattus frugivorus* though *R. norvegicus* was also common. A family of *R. rattus frugivorus* was captured the adult rat's serum agglutinated OXA at a titre of 1-160 one of the four young rats reacted at 1-40 the others were negative. By a lapse on the part of someone the author is shown as stating that the positive results show that *R. orientalis* disease does not exist among the rat population.

Seven local children aged 7-12 years were examined all gave positive reactions with OXA the titre was 1-160 in one 1-80 in two and 1-20 to 1-40 in the rest. The titres in five local adults were 1-40 in four and 1-20 in one. It seemed likely that all the local children must have been infected at some time that the adults have some degree of acquired immunity.

Of the 50 patients at Port \ 28 had actually been engaged on scrub clearing and the rest had come into close contact with scrub conditions. The suggested measures of prevention are clearing and burning all vegetation including the palm trees from camp sites and roadways by persons provided with mite proof clothing prohibiting entry to scrub land rat-proofing of stores and galleys and a vigorous anti rat campaign *John H D Megaw*

ZAIR A H. Scrub Typhus. *J Roy Nav Med Serv* 1944 July v 30 No 3 135-7

This is a brief general description of scrub typhus it is based presumably on cases seen at a Naval Hospital on an Indian-Ocean coast. Some statements in the paper need correction or qualification—for example the incubation period is about three weeks and the table of agglutination responses wrongly shows the same general type of reaction for tick typhus as for louse and flea typhus.

Among the methods of prevention that were used one would be extremely valuable in any place where it could be adopted this was the employment of bulldozers for scrub and jungle clearing. Where manual clearing is needed it is advised that the scrub should be sprayed with kerosene and burned as a preliminary measure. Mr H. CARTER Medical Entomologist for Ceylon is quoted as advising caution in undertaking rat-control operations trapping the rats alive and immersing them in kerosene was regarded as the only safe method. Mr Carter also recommended the regular removal of coconuts from the palm trees by indigenous labour as the best way of reducing the rat population in the neighbourhood of camps.

The case-fatality rate in the area was low but the morbidity and invaliding rates were high *John H D Megaw*

WEDD S. Lymphocytes Speckled and Plain an Unrecorded Blood Change in Scrub Typhus. *J Roy Nav Med Serv* 1944 July v 30 No 3 137-44 2 figs.

In a study of 400 blood films stained by Wright's or Leishman's method it was found that the average number of speckled lymphocytes was greatly increased in the post febrile stages of scrub typhus. Control counts were made in normal persons (89 counts) patients with sepsis (18) malaria (38) pulmonary tuberculosis (13) and dengue (19). In these conditions the average counts were much lower but in five cases of recent amoebic dysentery high counts were observed.

The speckled lymphocytes are those containing the azurophilic granules described by MICHAELIS and WOLFF in 1902 the granules are reddish in colour in smears stained by the above methods in normal blood such speckled cells were found to constitute on the average 18.6 per cent of the lymphocytes with a range of 5 to 37 per cent. Their actual numbers averaged 550 per cmm. with a range of 69 to 1,589. The figure of 1,200 was exceeded only three times in 89 counts and was taken as the upper normal limit. This limit was exceeded in all but three of the 22 patients who were examined within 40 days of the end of the fever stage of scrub typhus. The usual trend was towards a maximum count early in convalescence and a gradual fall to normal which was reached about 40 days after the end of the fever. In one exceptional case the count was 224 on the 13th day of convalescence and 1,670 on the 19th. The average of 76 counts in convalescence was 1,223 and the extreme limits were 104 and 6,700.

In a footnote it is stated that six patients were examined at another hospital on the 15th day of scrub typhus and that 41-69 per cent of the lymphocytes

were speckled on the 25th day the percentages ranged from 20 to 50 with an average of 39 the actual numbers ranged from 630 to 4 725 with an average of 2 100 In these cases the total leucocyte counts are mentioned they ranged from 10,800 to 24,200 per cmm.

The *O*1A agglutination titres of the patients during the febrile stages are not specified the highest titre recorded was 1 to 250—in three cases on the 24th, 17th, and 40th days respectively after the onset of the fever

In four out of five patients suffering from amoebic dysentery of recent development the count of speckled lymphocytes at some time exceeded 1,200 per cmm. and the author suggests that high counts may occur in other diseases.

[If the condition is found to be of definite significance, the name *arurophilosis* will be more convenient than increase in the speckled lymphocytes.]

John W D Meyer

WAR OFFICE. ARMY MED DEPT BULL. No 41 1944 Nov 1-2. Fluid Balance in Scrub Typhus.

According to recent information,* fluid retention may be well marked in severe cases of scrub typhus (*tsutsugamushi* disease) Therefore fluid intake and output need to be carefully balanced or the patient may suffer from the treatment intravenous fluids are seldom required in scrub typhus, and their ill-advised use may have special dangers In severe cases, it is not considered safe to force fluids by mouth beyond 4 or 5 pints daily

The cause of the fluid retention is still not clear and further investigations are being made. Meantime it has been noted that a well-marked diuresis, indicating the end of fluid retention, also foreshadows the onset of clinical improvement. In a recent series diuresis was noted in all of 11 severe cases and also in many milder infections In the severe cases, the average daily fluid intake before diuresis was 98.8 ounces and the average output 39.7 ounces. On the first day of diuresis the average intake was 119.1 ounces and the average output 95.7 ounces.

The diuresis in these severe cases is noted usually around the 14th day and about 3 to 4 days later the temperature settles below 99 deg F Along with the diuresis there is usually subjective improvement even before the temperature falls but the patient's appearance may show a deceptive worsening The fluid that has hitherto been retained hides the evidence that a good deal of flesh has been lost and the loss of flesh masks the occurrence of any oedema. Thus it will be understood how both abnormalities may pass unobserved and may indeed combine to give the patient a normal appearance

With the sudden diuresis the oedema is removed and the full extent of the wasting is abruptly and dramatically disclosed To all appearances the patient has taken a sudden turn for the worse he is profoundly weak his temperature has not settled, and his flesh has suddenly seemed to melt away Two observations may reassure the clinician—the presence of diuresis and the patient's own feelings. The confused mental state usually clears with the onset of diuresis and the patient himself is in no doubt that the change in his condition is decidedly for the better A few days later this will be confirmed when the temperature returns to normal.

We mention this phenomenon of fluid retention followed by diuresis in scrub typhus as a matter of interest that has not yet become part of the text book description. In general it is good advice to push fluids in all fevers and

those who nurse patients with epidemic and endemic typhus are usually so advised. Evidently it is also important to check the daily intake and output of fluids.

In severe cases of epidemic typhus there is often oliguria and diuresis may be well marked at some stage in the convalescence but here the fluid retention is usually associated with a raised blood urea and the lowest levels of blood pressure.

In scrub typhus the myocardium usually shows marked signs of weakness but evidence so far available shows that diuresis is not accompanied by any significant rise of blood pressure the blood urea is seldom high casts and red cells are not often seen in the urine and the kidneys of fatal cases do not often show obvious glomerular lesions. The underlying causes of the fluid retention and diuresis in scrub typhus may not be easily found but it would be of great value to have further clinical details about their occurrence and relation to other events in all forms of typhus. So there is an open and interesting field for further careful observation of a kind that requires neither specialized knowledge nor equipment.

CAVAZZI G. Segnalazione di cinque casi di febbre bottonosa sull'altopiano etiopico. [Report on Five Cases of Boutonneuse Fever in the Ethiopian Highlands.] *Boll Soc Ital di Med e Igiene Trop* (Sez Entrea) 1943 v 2, No 2, 5-9 [11 refs] English summary (4 lines)

These five cases occurred in Entrea and Asmara in all of them a black scab (tache noire) was observed at the site of the tick bite. The fever lasted 12 to 15 days and was relatively severe though none of the patients died. The onset was gradual and the termination was by rapid lysis. The rash appeared first on the trunk it spread rapidly to the rest of the body including the face palms and soles it was definitely papular and in two of the patients petechiae were seen. There was albuminuria with granular casts leucocytes and a few red blood cells in the urinary sediment.

The Weil Felix reaction was negative throughout the illness in one patient in the others the maximum titres were 1-80 1-160 1-160 and 1-640. In the one case in which a biological test was made there was no cross immunity with historic typhus.

The disease was regarded as being the same as Mediterranean boutonuse fever but the exact relationship to that disease and to tick bite fever remains to be worked out.

John W D Megaw

HELD A. Rheumatische Knötchen beim Wolhynienfieber ["Rheumatische" Nodules in Trench Fever] *Munch med Woch* 1944 Apr 21 v 91 No 15/16 193-4

The author states that in trench fever nodular or cord-like bodies are often found by careful examination of the scalp and other parts of the skin of the head also in other parts of the body to a lesser extent. These are tender to the touch and are believed to form the physical basis of the headaches shin bone pains etc. which are conspicuous features of the disease. When the nodules are effectively treated by massage preceded by warm applications the headaches and other pains disappear.

Acting on the view that the nodules indicate an allergic reaction the author tried non-specific protein therapy and obtained satisfactory results. This treatment was not given in the acute stages of the disease but in the chronic forms it was found that slight rises in temperature were not contra indications.

were speckled on the 25th day the percentages ranged from 20 to 50 with an average of 39 the actual numbers ranged from 650 to 4 725 with an average of 2,100. In these cases the total leucocyte counts are mentioned they ranged from 10,800 to 24,200 per cmm.

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The cause of the fluid retention is still not clear and further investigations are being made. Meantime it has been noted that a well-marked diuresis indicating the end of fluid retention, also foreshadows the onset of clinical improvement. In a recent series diuresis was noted in all of 11 severe cases and also in many milder infections. In the severe cases, the average daily fluid intake before diuresis was 98.8 ounces and the average output 39.7 ounces. On the first day of diuresis the average intake was 119.1 ounces and the average output 95.7 ounces.

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These five cases occurred in Eritrea and Asmara in all of them a black scab (tache noire) was observed at the site of the tick bite. The fever lasted 12 to 15 days and was relatively severe though none of the patients died. The onset was gradual and the termination was by rapid lysis. The rash appeared first on the trunk it spread rapidly to the rest of the body including the face palms and soles it was definitely papular and in two of the patients petechiae were seen. There was albuminuria with granular casts leucocytes and a few red blood cells in the urinary sediment.

The Weil Felix reaction was negative throughout the illness in one patient in the others the maximum titres were 1-80 1-160 1-160 and 1-640. In the one case in which a biological test was made there was no cross immunity with historic typhus.

The disease was regarded as being the same as Mediterranean boutonneuse fever but the exact relationship to that disease and to tick bite fever remains to be worked out.

John W D Megaw

HELD A. Rheumatische Knötchen beim Wollhymenieber ["Rheumatic Nodules in Trench Fever"] *Münch med Woch* 1944 Apr 21 v 91 No 15/16 183-4

The author states that in trench fever nodular or cord-like bodies are often found by careful examination of the scalp and other parts of the skin of the head also in other parts of the body to a lesser extent. These are tender to the touch and are believed to form the physical basis of the headaches shin bone pains etc. which are conspicuous features of the disease. When the nodules are effectively treated by massage preceded by warm applications the headaches and other pains disappear.

Acting on the view that the nodules indicate an allergic reaction the author tried non-specific protein therapy and obtained satisfactory results. This treatment was not given in the acute stages of the disease but in the chronic forms it was found that slight rises in temperature were not contra indications.

in fact the recurring attacks of fever were often cut short. In the early stages large doses of pyramidon (amidopyrine) were of considerable benefit.

John W. D. Megaw

YELLOW FEVER.

BOSHILL MAXRIQUE J & OSORNO-MESA E. Observations on the Epidemiology of Jungle Yellow Fever in Santander and Boyacá, Colombia, September 1941 to April, 1942. *Amer J Hyg* 1944 Sept. v 40 No. 2, 170-81 3 maps.

The authors have collected large numbers of mosquitoes in the Colombian mountain districts of San Vicente de Chucurí (Santander del Sur) and Muzo (Boyacá) and tested their infectivity by feeding them on *rhesus* monkeys and also by inoculating the ground-up contents of the mosquitoes into the brains of mice.

Yellow fever virus was demonstrated in two batches of *Haemagogus capricornis* Lutz, caught in Guincha and also in two batches from San Isidro districts south of Muzo. In one instance a monkey bitten by these mosquitoes became immunized, although mouse inoculation failed to demonstrate the virus.

A batch containing two *Aedes leucoclarvus* and six *A. downsi* produced infection which is considered to be probably due to the former species, a proved carrier. Possible transmitters were *Haemagogus cygnus* Theobald and *H. lucifer* Howard, Dyar and Knab.

A few marsupials were caught including *Didelphys Metachirus*, *Caluromys* and *Chironectes*. Two protective sera were found out of 14 examined but the animals could not be kept alive for confirmatory tests.

The authors found that *Haemagogus* travels considerable distances from its breeding places; also virus-carrying mosquitoes were caught in localities remote from the probable sources of human infection. This species is strongly phototropic and in mountain districts during the afternoon travels up the slopes away from the deeper parts of valleys which are in the shade. There is also a tendency for *Haemagogus* when seeking blood, to follow human beings and mules some distance from the forest.

It is emphasized that the yellow fever virus isolated in these experiments was of purely jungle origin and the infected mosquitoes were caught in uninhabited and virgin jungle distant from any contact with man. E. Hinde

PERLOWAGORA Alma & LENNETTE E. H. Observations on the possible Usefulness of the Complement Fixation Test in the Early Diagnosis of Yellow Fever. *Amer J Trop Med* 1944 July, v 24 No. 4 225-44 [31 refs.]

The authors previously described a complement fixation test for the diagnosis of yellow fever in man and animals (see this *Bulletin* 1944 v 41 211) and in the present paper give the results of its application in 18 monkeys, *Macaca mulatta* and 31 marmosets, *Callithrix jacchus* infected either with the Asibi strain of yellow fever virus or with one of the South American jungle strains. In this test the antigen is present in the serum of infected animals; the antibody in the serum of animals recently recovered from the infection.

In a preliminary experiment complement fixing antigen was found without exception in the sera of 6 monkeys and 17 marmosets infected with yellow fever virus, the blood being collected at, or just prior to death. Subsequently 12 monkeys and 14 marmosets were inoculated with various strains of virus and the serum examined daily in the case of the monkeys, and at various intervals in

the case of the marmosets. The results are given in tabular form and indicate that occasionally the antigen might appear in the blood on the second day after inoculation especially in marmosets. As far as can be judged the time of appearance in the blood was roughly dependent on the length of the interval between inoculation and death of the animal when this period was three to five days the antigen usually appeared on the third day and when longer the antigen appeared one to three days later. In four monkeys and one marmoset which survived infection antigen was not found in any of the serum tested.

There was no obvious correlation between the febrile reaction and appearance of antigen also the presence of relatively large amounts of circulating yellow fever virus in three monkeys and a marmoset which survived, was not accompanied by the development of antigen. This would seem to indicate that this property is associated with a factor distinct from the virus. In 10 out of 37 animals a post mortem diagnosis of yellow fever virus infection could not be made by histological examination of the liver although it was made during life by examination of the serum for complement fixing antigen. From these results it may be possible to use this test for the diagnosis of the disease in human cases of yellow fever.

E Hindle

SELLARDS A W & McCANN W S Choline Hydrochloride in Experimental Yellow Fever in Rhesus Monkeys. *U.S. Nat. Med. Bull.* 1944 Sept. v. 43 No 3 420-22.

The authors tested the effects of choline hydrochloride by mouth on the course of the infection in rhesus monkeys *Macaca mulatta* inoculated with the Dakar strain of yellow fever virus which for 15 years had exhibited uniformly lethal properties.

TABLE I—Summary of results.

Lot 1—Choline started about 2 hours prior to injection of virus

Rhesus	Choline		No. of days of continuous fever	Result
	Mgm. per kilo	No. of days		
462	80	13	6	Recovery
463	80	12	none	Recovery
461	160	12	none	Recovery
465	160	4	2	DD—4th day
464	control		2	DD—3rd day
466	control		3	DD—4th day

Lot 2—Choline started 3 days prior to injection of virus

Rhesus	Choline		No. of days of continuous fever	Result
	Mgm. per kilo	No. of days		
467	80	3*	1	DD—4th day
468	80	4*	none	Recovery
469	160	6*†	3	Recovery
470	160	4*	2	DD—4th day
471	control		2	DD—4th day
472	control		3	DD—6th day

* Exclusive of 3 preliminary injections.

† Continued for 6 additional days on 80 mgm. per kilo.

In the first experiment six monkeys were inoculated with yellow fever virus and four were treated with the choline hydrochloride administered by means of a stomach tube. The drug was given two hours before the inoculation of virus and repeated daily up to 13 days in the case of the survivors. Two monkeys received 80 mgm. per kilo daily and both survived, and two received 160 mgm. per kilo daily and one survived. Both controls and the other treated monkey died on the 3rd or 4th day. In a second experiment with six monkeys, four being treated and two kept as controls treatment in the same manner was begun three days before the injection of virus and two of the four treated monkeys survived. The experiments are summarized in the table above.

Thus out of eight monkeys receiving choline hydrochloride three died and five survived. Even in the case of these three dead monkeys examination of the liver showed some evidence of a reparative process, with much less disorganization of the architecture and more proliferation in the perportal spaces.

[The death of Dr. Seillards interrupted the continuation of these experiments, which indicate the possibility that the liver may be protected against the action of yellow fever virus by the oral administration of choline.] *E. Hindle*

WAR OFFICE, ARMY MED DEPT BULL. No. 41 1944 Nov 2-3. Control of Yellow Fever

Control of yellow fever was always a problem of preventive medicine of world wide importance. Various war conditions especially the passage of numerous aircraft through endemic zones, have added to the difficulties of control and increased its necessity. The disease transmitted by the bite of *Aedes aegypti* and related mosquitoes, was a serious danger to early colonists in West Africa. In 1826 out of a garrison of 535 soldiers 115 died in two months and of the first detachment of troops to occupy Cape Coast Castle (West Africa) in 1823 only one was alive in the following year*. In the Anglo-Egyptian Sudan in 1940-41 an epidemic caused at least 20 000 cases with 2,000 deaths.

"Many investigators gave their lives in a long series of devoted researches before it was finally established in 1923 that the disease was due to a filterable virus. In following years a safe and effective vaccine was developed that conferred good immunity by one inoculation with living virus modified by passage through animals and developing eggs. Systematic use of this vaccine is to-day one of the chief means of controlling the disease. A brief general outline of this aspect may be of value.

Yellow fever is endemic in West Africa and certain parts of South America, especially Brazil. Certain other territories appear to offer all the necessary conditions for spread of the disease but have so far remained free these areas include Egypt and India. Whatever the reasons for their freedom, it is our object to avoid all possible risks of introducing the disease to these countries from the endemic zones.

In days when travel was slow the risk of spreading the disease beyond the endemic areas was not great. But to-day an aircraft can carry living infected mosquitoes or passengers incubating the disease in a matter of hours from a yellow fever area to a distant one and the risk of spreading the disease is, therefore real. When air traffic was on a small scale it could be regulated and directed from specially constructed (anti-malaria) aerodromes with facilities for controlling mosquito breeding screening huts disinfecting aircraft and putting passengers in quarantine if there was a risk of their having been exposed to infection. These measures are still important but increased air traffic and great extensions to aerodromes have made it difficult to apply these measures of control as effectively as before.

But the vaccine has changed the whole problem. If all passengers are immune they can neither suffer from the disease nor transmit it. If all who live or work on or near the aerodrome are also immunized the mosquitoes that bite them cannot become infected. After vaccination immunity takes 7 to 10 days to develop fully and it lasts for 4 years. Therefore intending passengers must be immunized not less than 10 days or more than 4 years before they are allowed to proceed by air from an endemic to a safe area where the disease might develop. This means immunization of all air passengers who will pass through endemic zones of yellow fever.

No biological method of control can ensure complete safety, but the sum of all the measures enormously weights the balance against transmission of the virus to new territories. Manufacture, storage and handling of the vaccine requires an appreciation of certain technical facts concerning its properties, therefore yellow fever immunization is done only at a limited number of special centres where suitably trained staff are available. The use of vaccine that was not fully potent would confer a false sense of security and might precipitate a disaster of international significance.

WILLIAMS C. L. Yellow Fever Control during the War. *Armer J Trop Med* 1944 July, v 24 No. 4 245-7

The potential danger of introduction of yellow fever into the southern United States has been increased by international air travel and especially by the dislocations and confusions of war. The author outlines the quarantine and control measures that have been introduced by the U.S. Public Health Service to meet war conditions. These follow the usual lines but in connexion with control it is mentioned that a stock of one half million or more doses of yellow fever vaccine is maintained at its laboratories in Hamilton Montana. This vaccine could be sent at short notice by airplane to any locality where it was considered necessary to institute general vaccination. The Public Health vaccine does not contain human serum and therefore its use has not been attended by any outbreaks of jaundice.

E. Handle

DENGUE AND SANDFLY FEVER.

COLLINS J. D. Colorado Tick Fever. Report of Thirty-Nine Cases. *Bull. U.S. Army Med. Dept.* 1944 Sept. No 80 81-5 3 figs

All the 39 patients whose cases are dealt with in this paper had bivouacked for several days before the onset of the fever in a tick-infested region near Colorado Springs. All the ticks found on the patients were *Dermacentor andersoni*. There was a definite history of tick bite in 27 of the cases and in five others ticks had been found on the body or clothing. The average time between tick bite and onset was 4.7 days.

The average duration of the first spell of fever was 1.2 days, of the afebrile interval 2.0 days and of the second spell of fever 1.7 days. A faint macular rash was seen in one patient.

The chief symptoms were—fever in all, chills in 36, headache in 30, muscle aches in 25, weakness in 20, and cough in 14. The leucocyte count was less than 2,000 in 2, and 2,000-4,000 in 25. In the 5 cases with counts of more than 6,000 the blood was examined late in the second spell of fever or in convalescence. In only one case there was a single spell of fever. There was no evidence of person-to-person transmission in any of the cases.

The disease is stated to differ clinically from dengue in the less severe involvement of the bones and joints and the absence of rash. No other difference could be detected. [See also this *Bulletin* 1941 v 38 694] *John W D Meyer*

FLORIO L. STEWART Mabel O & McGRACK E. R. The Experimental Transmission of Colorado Tick Fever *J Exper Med* 1944 Sept. 1 v 80, No. 3 165-88 6 text figs & 2 figs. on 1 pl.

Colorado tick fever was recognized as a special disease by BECKER in 1930. The name is regarded by the authors as misleading because the disease is known to occur in the same western area as Rocky Mountain spotted fever. The fever has been studied by TOPPING and his colleagues [see this *Bulletin* 1941 v 38 694]. It closely resembles dengue fever except for the absence of rash, but dengue is unknown in the region of its endemicity unless indeed we are dealing with a tick borne variety of this disease. There is very strong though purely circumstantial, evidence that the transmitting vector is *Dermacentor andersoni*.

In the present investigation each of 5 volunteers received a subcutaneous injection of 4 cc. of serum taken from a patient during the first or second spell of fever. Four of the volunteers developed typical attacks after incubation periods of three or four days. Serum from the volunteers was used in the same way to initiate the inoculation of eight other persons, all of whom developed similar attacks, though in two cases the incubation period was five days, and in one it was 10 days. In the course of the experiments the infection was passaged six times in succession from person to person without obvious change in its characters of virulence.

Three of the patients were tested for immunity 9-11 months later. Two of them developed severe headache without fever four days after the test inoculation. The other had no symptoms.

Four of the persons who were inoculated had previously been immunized against Rocky Mountain spotted fever by double the usual number of injections of tick vaccine. Three of them developed typical attacks of Colorado tick fever, and the fourth who came from a region of high endemicity had slight fever and headache lasting three hours.

Unsuccessful attempts were made to transmit infection to five volunteers by the bites of the offspring of 12 laboratory bred ticks (*D. andersoni*) which had fed on two of the experimentally-infected patients for 8-11 days beginning from the onset of the fever. Two of these volunteers were tested later and were found to be completely susceptible to inoculation with infective serum.

Serum from an experimentally infected patient was used to initiate a series of transfers through golden hamsters (*Cricetus auratus*). The only obvious sign of the disease in these animals was leucopenia: the leucocyte count of the animals fell by the 3rd or 4th day after inoculation from an average of 8,090 to one of 4,540. Serum from a hamster at the 7th passage was injected into a volunteer who developed a typical attack of greater severity than any of the others that were observed.

Now that hamsters have been found suitable for the passage of the infection further work is contemplated with the object of determining whether the disease is related to dengue fever.

The blood changes observed in the experimental cases were found to be remarkably similar to those of dengue fever as described by SUTTONS and his colleagues in 1931 [this *Bulletin* 1931 v 28 613]. The total leucocyte count fell to about 2,000 at the onset of the second spell of fever and the Schilling haemogram showed a pronounced deviation to the left: sometimes the band-forms were more numerous than the segmented. In early convalescence a few

peculiar large lymphocytes were often seen these had 2-8 small round bodies staining like nuclei in the cytoplasm.

[Colorado tick fever may turn out to have more than local importance. As the authors rightly suggest the name is misleading and for this reason cases have been missed in other parts of the world just as happened in connexion with Rocky Mountain spotted fever whose name is even more unsuitable. The close clinical resemblance to dengue fever is a very striking feature of the disease and the present experiments tend to support the tentative suggestion already made by the reviewer that it may be a tick borne fever of the dengue group. If so its relationship to mosquito-borne dengue would be somewhat analogous to that existing between tick borne and louse-borne typhus.]

Attempts will doubtless be made to transmit the virus of dengue and sandfly fever through the hamster and it is to be hoped that these will be made with animals that have not been exposed to the risk of naturally acquired infection and in localities which are known to be free from these diseases.]

John W D Megaw

STEWART Mabel O FLORIO L & MURRAY E R Hematological Findings in the Golden Hamster (*Cricetus auratus*) *J Exper Med* 1944 Sept. 1 v 80 No 3 189-96

PHILIP C B PAUL J R & SABIN A B Dimethyl Phthalate as a Repellent in Control of Phlebotomus (Pappataci or Sandfly) Fever *War Medicine* Chicago 1944 July v 6 No 1 27-33 8 figs [Refs in footnotes]

Dimethyl phthalate is the most widely used repellent at the present time against mosquitoes and other blood-sucking insects. That its use will have some effect in reducing the incidence of malaria is inferred from the fact that it will prevent the biting of mosquitoes for several hours. The authors have succeeded in obtaining more direct evidence of its efficacy in controlling sandfly fever. In a barracks containing some 170 American soldiers on the outskirts of Cairo the use of this repellent was the sole preventive measure employed during a period of five weeks in the epidemic season. Bottles of dimethyl phthalate and of distilled water with or without a few drops of methylthionine chloride were supplied to men occupying alternate beds. Five cc. of repellent was used per man per day this amount being spread as a thin film just before the man retired on forehead, sides of face neck hands and forearms and any other exposed surfaces. Of the men receiving the repellent 42 per cent. reported relief from bites of those receiving the control solution 12 per cent. reported relief. Of the men receiving the repellent two acquired sandfly fever but both admitted that they had failed to apply it for several consecutive nights prior to contracting the disease. Of those receiving the control solution or no solution 12 acquired sandfly fever.

V B Wigglesworth.

CHOLERA

YACOB M Epidemiology of Cholera in the Punjab *Indian Med Gaz* 1944 Aug v 79 No 8 383-90 2 charts & 2 maps. [11 refs.]

In this interesting review of the epidemiology of cholera the author insists that the province of the Punjab is a non-endemic cholera area. It is like Europe the Netherlands Indies and Japan a sufferer from the menace of its eastern or western neighbours. Perhaps we might not agree that British India

is so entirely and centrally black as it is painted in Map 1 of this article and contend that China or even the Russian Don region have some blame for the endemicity and potential epidemicity of cholera. The main reasons adduced for the continuance of cholera are the habits of the people, the prevalence of massed pilgrimage and probably also a climatic environmental factor. It may not be too much to hope that these are all capable of being altered, regulated or countered by appropriate measures. The cases of Japan and Java with more autocratic rule or more docile populations might be cited in this connexion. The Western Punjab is not entirely free from the danger due to a great concourse of pilgrims such as that associated with the solar eclipse at Kurukshetra in the Karnal district and it is significant to remark that the most recent solar eclipse fair at Thanesar held in 1941 passed off without a single case of cholera. The fair was attended by approximately 500 000 pilgrims. This would appear to have been a triumph for the Punjab health organization. When however he deals with the pilgrim centres of Hardwar Benares and Allahabad, the author seems to align himself with the contention that nothing less than protection by inoculation of the pilgrims going to and from the fairs can possibly stop the regularly occurring epidemics. A point on which he briefly touches and which is extremely important from the point of view of insistence on and enforcement of quarantine is the identification of the true epidemic cholera vibrio. Apart from the epidemic proof itself this has been largely narrowed down to the possession of a heat-stable antigen specific agglutinability and certain biochemical sugar reactions. Two useful maps two equally useful charts and a table give a rapid review of the distribution and mortality of cholera according to province and seasons of the year.

W F Harvey

TANG F F, CHU C. M. & WONG Y. W. A Study of *Vibrio cholerae* isolated from the 1942 Kunming Epidemic, with special reference to Serological Types. *Indian J Med Res* 1944 May v 32, No 1 1-8

For several months during the epidemic only the Inaba type of vibrio was found but towards the end some Ogawa vibrios were encountered. Altogether 69 strains of isolated vibrio were typed and gave percentage proportions of 93 Inaba and 7 Ogawa. Two strains were inagglutinable but no intermediate strains were met with.

W F Harvey

MISRA, K. N. Treatment of Cholera and Diarrhoea. Observations on 210 Cases. *J Indian Med Ass* 1944 July v 13 No 10 279-282.

All of these 210 patients came to hospital with the diagnosis of cholera and the bacteriological examination of the stools showed 153 to be cholera positive and 35 negative. The stools in the remaining 22 could not be examined. For purposes of analysis the cholera negative and the non-examined were regarded as cases of severe diarrhoea only. Treatment was carried out on a comparison basis and thus was —(a) with $\frac{1}{2}$ gram calomel and 5 grains sod bicarb. every half hour with the addition of alkaline saline, hypertonic saline and normal saline plus 5 per cent glucose as circumstances demanded (b) with cholera phage and sod bicarb drink (1 dr to a pint) (c) with sulphapyridine 3 gm. every 3 hours for 24 hours then 2 gm [3-hourly?] up to a total of 9 gm and alkaline mixture (d) with sulphaguanidine tablets in the doses of 10 tablets of 0.5 gm. on admission continuance at the rate of 4 tablets every six hours till the stools per day became 5 or less and then 2 tablets every 8 hours till cure. The conclusions come to are —Group D gave the best results with only 1 death out of 18 cases treated. In mild (early) cases treatment with fractional doses of calomel or Phage solution gave a very good percentage or

cure but was not reliable for severe (late) cases Group C showed no better results than the other three and was more expensive than either Group A or Group B treatment

BOSE B C & AIRUJA H L. Detection of Pyrogens in Fluids by Biological Methods *Indian J Med Res* 1944 May 32 No 1 9-14 2 graphs

Solutions for intravenous injection should be free of pyrogenic organisms. Tests for freedom are (1) the hyperpyrexia test and (2) the leucopenia test. Among the most useful findings in this paper are the precautions necessary to prevent physiological variation of body temperature and the range of that variation. When precautions are taken for the reading of temperatures such as (1) the use of rabbits accustomed to handling (2) the use of fasting animals and (3) the insertion of the thermometer to a constant level of $\frac{1}{2}$ inch from the anal ring the day to-day variation does not exceed 0.6°F . Two organisms one chromogenic and the other non-chromogenic were isolated from reservoir water and were found to be notably pyrogenic. These were used to test the validity of the ordinary tests of pyrogenicity. As a result the hyperpyrexia test has been found fairly satisfactory and the leucopenia test unsuitable

W F Harvey

BACILLARY DYSENTERY

BLOOM H. Dysentery in British Prisoners of War *Lancet* 1944 Oct 28 558-60

This is a somewhat tragic account of sufferings undergone by British prisoners of war in Italian prison camps in North Africa. From October 1942 to April 1943 the author was in medical charge of British prisoners in an Italian hospital. All had been captured in the second fortnight of June 1942 during the retreat from Tobruk. Herded in cages in various parts of Libya and Tripolitania they had no shelter and existed in semi tropical heat. The diet was subminimal and consisted mainly of a handful of macaroni 8 oz of coarse brown bread, a small piece of cheese daily with about an ounce of meat twice weekly. No attempts were made to provide proper sanitation a few unprotected trenches in the camps were soon filled and overflowed. Flies abounded and in some camps 90 per cent of the men developed dysentery many becoming so weak from starvation and incontinence that they were found lying beside the overflowing latrines. In one camp during July 1942 19 out of 3 000 men died in another during the three months July to September 100 died. This mortality beginning within a month of the capture of men who were fighting fit gives one some idea of the appalling conditions in North Africa. Some of the worst cases were taken over to Italy in batches in October and November under dreadful conditions and in all kinds of ships most of them were desperately ill and emaciated. In Caserta Hospital the deaths from dysentery apart from wounds were 36 in October 45 in November 42 in December 1942 10 in January 1943 4 in February and 2 in March and April. In all about 200 men were treated by the author who was himself a prisoner and eventually he was given a free hand (with the result that the frequent Italian diagnosis of nephritis for anasarca due to protein-deficiency was discarded). Sisters of Mercy and Red Cross nurses obtained everything possible in a country depleted of necessities by the occupying Germans. The only facility for investigation apart from clinical study was a laboratory under the

charge of an expert pathologist to which the author was not allowed access, and which examined only faeces. All the men were extremely weak and emaciated; many were unable to walk, and all were infested with lice to which they were remarkably insensitive. With sunken eyes surrounded by wary periorbital tissues and with symptoms of severe dysentery (with the passage of 20 or more daily motions, often accompanied by incontinence) they presented a pathetic picture. Deficiency states were manifested as oedema of varying severity, atrophy and pigmentation of the skin, and loss of deep reflexes. Other symptoms of vitamin deficiencies appeared during the next three months.

Vitamin-A deficiency—The high incidence of intercurrent infections suggested lack of vitamin A. These infections included a ten-day periodic fever suggestive of trench fever and cases of epidemic hepatitis. Six cases of night-blindness were identified, and there were probably more.

Vitamin-B complex deficiency—Symptoms of beriberi were present in all except Indians and South African natives. These consisted of pains and tenderness in the limbs, muscular atrophy (contractures in one) and loss of peripheral reflexes. Cardiac involvement was apparent in 8; acute neuritis involving pelvic visceral and somatic nerves in 3. Many of the men showed some or all the signs of ariboflavinosis—such as seborrhoeic dermatitis, vascularization of the cornea and unequal pupils (in 2). Pellagrous symptoms consisted of pigmentation and atrophy of the skin of shins and wrists. Many of the men showed symptoms of progressive melancholia.

Vitamin-C deficiency—Some of the worst cases had haemorrhage from the intestine and kidneys and petechial haemorrhages in the skin over various parts of the body even when the consumption of lemons and oranges was high.

Vitamin-D deficiency—Only those most seriously ill showed deficiency of vitamin D. The teeth of several turned black. In one case six attacks of tetany with carpopedal spasm preceded death. Two men showed a strongly positive Chvostek's sign.

In none of the men was the onset of dysentery associated with fever. In a few it commenced with blood in the faeces, but in others the appearance of blood was delayed and persisted for months with mucus and pus. Although *Entamoeba histolytica* was reported in all cases, emetine injections exerted no influence in the clinical sense. The major part of the infection appeared to be non-specific, and remained unresponsive to specific treatment.

For many months after the onset of their illness these men continued to receive the Italian ration of rice, cheese, milk and coarse wholemeal bread; meat was being withheld. It soon became obvious that the essential factor in treatment was the diet. Brown bread was therefore entirely replaced by porridge and other foods from Red Cross parcels and the improvement in patients on this diet, as compared with the bread-eaters, became obvious. Eventually 8 oz. of meat were added daily and not only did the bowel symptoms improve, but symptoms of vitamin-B deficiency gradually disappeared, with the lifting of the mental depression. Milk in large quantities was found to pass through the damaged bowel in large undigested masses.

Vitamin food deficiencies had to be made up from the diet and from Red Cross parcels. Local treatment by colonic washouts had no apparent effect.

Sulphaguanidine, which became available in February 1943, was given to 9 of the worst cases with undoubted effect on 7 after an intensive course. Intravenous glucose and saline, by long-continued drip, never succeeded, probably because of the toxic condition of the heart, but intramuscular injections of 250 cc. of glucose saline twice daily were well tolerated and gave good results. The author was soon convinced that indiscriminate dispensing of "salts" to cases of dysentery is a most dangerous practice and caused inevitable exacerbation of diarrhoea. [Those who remember somewhat similar but not

such barbarously extreme occurrences in the last war will recognize the clinical condition as the aftermath of bacillary dysentery in exhausted and partially starved men. At that time we were ignorant of the syndromes caused by the vitamin-deficiencies but by analogy it seems extremely doubtful whether the laboratory reports of the invariable presence of *E. histolytica* were correct. The acknowledged specific action of sulphaguandine would suggest that the original infection was bacillary and not amoebic in origin.]

Howat H T **Fatty Diarrhoea In Chronic and Relapsing Dysentery** *Lancet* 1944 Oct. 28 560-61 P Manson Bahr

In the Middle East chronic and relapsing dysenteries of varied aetiology have been complicated by stomatitis and steatorrhoea.

The earlier cases were seen in prisoners of war and others who gave a history in addition to inadequately treated dysentery of inadequate dietary. Later a similar syndrome occurred in British soldiers whose diet had been balanced and well-controlled. At one period in 1943 six such cases were under treatment in one fifty bed dysentery ward. During the acute phase stomatitis and sore tongue attributed to nicotinic acid deficiency were common and rapid relief followed the giving of this drug in large doses by mouth. In British soldiers riboflavin deficiency was not seen nor were oedema or skin haemorrhages. Achlorhydria or hypochlorhydria was the rule. A mild hypochromia was usual but megalocytic anaemia was noted in only one long standing case of this group. The stools were increased in number, bulk and weight, offensive, frothy and greasy of the sprue type with excess of hydrolysed fat.

Hydrochloric acid and nicotinic acid in large doses by the mouth produced no alteration in the stools. In a few cases to which it was given in adequate dosage parenteral liver extract caused amelioration of the acute features but relapse ensued when it was discontinued too soon. Clinically in sprue as in fatty diarrhoea associated with colonic disease evidence of deficiency in various factors of the vitamin B₂ group is sometimes observed but in many cases multiple factors are involved which are difficult to dissociate on clinical grounds. The factors in the B₂ complex are interdependent and deficiency of one may lead to imperfect action of others. A clue to the rôle played by chronic diarrhoea may be found in the cases in which the diet had been adequate throughout. These patients had been treated with sulphaguandine and in some the relationship of the onset of fatty diarrhoea to this treatment was striking.

It is suggested that this drug may be a factor in the production of a conditioned deficiency by inhibiting the growth of commensal organisms in the bowel. It has been shown experimentally that sulphaguandine and also succinyl sulphathiazole over long periods can reduce the bacterial flora of the bowel thus inhibiting synthesis of many essential factors—such as thiamin, members of the B₂ complex—pantothenic acid, folic acid and biotin—riboflavin, nicotinic acid, inositol and vitamin K. Possibly the host relies on this synthesis for augmentation of the natural supplies of these vitamins.

It is suggested that the large-scale use of sulphaguandine in the treatment of bacillary dysentery may explain the apparent rise in incidence of fatty diarrhoea in British soldiers with this disease. In one case the onset of frank pellagra was precipitated by an exacerbation of Flexner dysentery. [It would be better before accepting this hypothesis *in toto* to compare the incidence of steatorrhoea in a group of post-dysenterics untreated by sulphaguandine. The reviewer has for many years recorded the supervention of the sprue syndrome in patients convalescent from bacillary dysentery.]

P Manson Bahr

FERRIMAN D G & MACKENZIE G K Comparison of Sulphonamides in Bacillary Dysentery *Lancet*, 1944 Nov 25 687-8.

The authors compared the effects of giving sulphamidamide sulphaguanidine and sulphathiazole respectively in bacillary dysentery in a R.A.F. hospital in West Africa. There were 56 cases and in 27 of them dysentery bacilli (unspecified) were isolated. The measure of efficiency of the drug used was the time taken for the stools to return to normal in cases which responded rapidly constipation for 24 hours was often the first intimation of recovery and this period was taken as half a day in the reckoning (see below). The dosage was sulphaguanidine initial dose 6 gm. then 3 gm. four-hourly sulphathiazole and sulphamidamide initial dose 2 gm. then 1 gm. four-hourly when the stools became normal the treatment was given six-hourly for 6 days or more. The results may be tabulated as follows —

	Sulphamidamide	Sulphaguanidine	Sulphathiazole
Average time to recovery days	3.8 (18 cases)	3.4 (18 cases)	2.7 (20 cases)
Cases taking longer than 2 days to recovery	3½-5 (13 cases)	3½-5 (10 cases)	3½ (2 cases)

The authors conclude that sulphathiazole is more effective than sulphaguanidine and that sulphamidamide is less effective than the other two drugs. They decided that sulphaguanidine was the choice in mild cases and in cases with dehydration and consequent risk of renal complications. Sulphathiazole was valuable in other severe cases notably because it relieved discomfort rapidly. They tried sulphapyridine but gave it up because it caused vomiting. Papers by PATTISON (*this Bulletin* 1943 v 40 241 and by SCADDING (*ibid.*, 1944 v 41 755) are referred to.

J F Corson

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

MORGAN C \ Amoebiasis some Difficulties of Diagnosis. *Brit Med J* 1944 Dec. 2, 721-2 2 figs

Amoebiasis produces diagnostic pitfalls and surprises. Colonic and rectal tumours, anal and perianal ulceration, recurrent colitis enigmatic liver abscess are numbered amongst its sequelae.

There is evidence that the chance of cure bears an inverse relation to duration of symptoms before emetive treatment is commenced.

Sigmoidoscopic appearances are varied and the lesions are often minute and easily missed. In addition to the typical discrete ulcers other changes may be seen, including scattered petechial haemorrhages without ulceration deeply inflamed hypertrophic oedematous mucosa, which may be nodular to the touch a large, solitary irregular indurated ulcer infiltrating the rectal wall or diffuse proctitis limited to the rectum.

The association of bacillary with amoebic dysentery should be remembered. The diffuse inflammation with irregular erosions or large irregular flame-shaped submucous haemorrhages, may overshadow amoebic lesions but sometimes discrete clean-cut ulcers identical in appearance with those of amoebiasis,

may be seen in bacillary dysentery. Not infrequently sigmoidoscopic findings are indefinite so that re-examination after a course of sulphaguanidine or it may be emetine may prove necessary.

In amoebiasis secondary manifestations may constitute the first indication of infection. A case is reported of an abscess and empyema treated by aspiration and rib resection. 22 days later rectal examination revealed an indurated hypertrophic ulcer which was diagnosed as an amoeboma and amoebae were cultured from the faeces. The discharge from the empyema quickly cleared up under emetine treatment. Amoeboma (or amoebic granuloma) results from repeated amoebic invasion of the colon with superadded pyogenic infection and may produce a progressive inflammatory lesion. The inflammatory process spreads through the bowel wall into the pericolic and perirectal fat and infiltrates surrounding structures. The resulting tumour consists of fibrous tissue granulations and varying degrees of ulceration. There is considerable round-cell infiltration. Lymphocytes and eosinophils are present in large numbers. Typical amoebic ulcers may be present or no evidence of amoebiasis may be forthcoming. The usual sites are the rectum recto-sigmoid junction and caecum. When the mass is situated on the recto-sigmoid junction or in the rectal ampulla the patient complains of tenesmus and may pass blood and mucus.

Diagnosis from carcinoma of the rectum is difficult sometimes impossible by digital examination or by sigmoidoscopy. The dark red nodular and ulcerated lesion looks like a carcinoma and moreover a smooth rounded non ulcerated mass cannot be distinguished by these means from submucous spread of carcinoma. Even when amoebae are found in the faeces carcinoma cannot be excluded until a biopsy has been made. Carcinoma and amoeboma may coexist. In the early stages of tumour formation the whole mass will melt away after emetine treatment. A previous history of dysentery is suggestive as in one case with pain in the anal region and retention of urine. Sigmoidoscopy showed a firm irregular tumour on the posterior rectal wall. After a course of emetine the tumour totally disappeared within one month.

But when the amoebic lesion has been present for a long period the superadded result of secondary infection fibrosis and colonic distortion may prevent the disappearance of the mass after anti-amoebic treatment. In such cases excision of the tumour may be necessary on account of obstructive symptoms or because it may be impossible to exclude carcinoma.

A case is quoted of a man of 44 with dysenteric history with increasing recurrent abdominal colic and pain in the right iliac fossa anorexia and slight fever. A large tender mass was palpable in the right iliac fossa. Amoebic ulcers were found in the rectum and active *E. histolytica* in the faeces. A large inflamed mass was found in the caecum attached to the anterior and posterior abdominal walls with adherent coils of small intestine. Ileo-caecal resection lateral ileo-colic anastomosis and drainage of retroperitoneal tissues became necessary. With 8 grains of emetine injected and blood transfusions and iron for secondary anaemia uneventful recovery ensued. Even after removal the tumour was thought to be an amoeboma till microscopic examination showed it to be an adenocarcinoma grade II with mucoid degeneration.

Differential diagnosis between amoebic typhlitis acute appendicitis and abscess of the appendix presents difficulties. The typical history of appendicitis may not be obtained and obstruction of the lumen of the appendix may result from amoebic infection. Operation is undesirable in the presence of un complicated active amoebiasis of the caecum and appendix, but in spite of this surgical treatment must not be delayed if signs of obstructive appendicitis are encountered within the first 24 to 36 hours whether the patient has amoebic dysentery or not. When a mass is palpable in the right iliac fossa, though it may prove impossible to distinguish between an appendix abscess and amoebiasis

are then able to exert their damaging effect on the liver. The assumption that bacterial toxins are responsible for functional liver damage in amoebic dysentery is in accord with the experience that such toxins contribute to the development of cirrhosis in experimental animals. A further proof that not the amoebic but the accompanying bacterial infection interferes with hippuric-acid synthetase in many cases of amoebic dysentery is the fact that amoebic hepatitis affects the liver functions less. These results confirm the view that liver function tests rarely help in establishing an early diagnosis of amoebic hepatic involvement. A warning is issued that beneficial effects of therapeutic emetine dosage on liver function should not encourage the use of this drug in other forms of hepatic disease.

P. Manson Bahr

BRESH, S. On the Treatment of Chronic Amoebiasis. *Acta Med Orientalia (Palestine & Near East Med J)* 1944 July-Aug v 3 No. 4 107-11

Chronic amoebic infection of the intestinal tract is one of the most important therapeutic problems facing the medical practitioner in the Middle East. The condition is common in Palestine and constitutes 5-10 per cent. of admissions and is the cause of about one-third of the gastrointestinal complaints met with in hospital practice. Methods of treatment are all based upon the administration of drugs derived from ipecacuanha, iodine or arsenic. It soon became evident that though emetine is efficient in the treatment of acute amoebic dysentery and of its extra intestinal complications its use in chronic amoebiasis was disappointing. Heroic doses have been given intramuscularly and even intravenously with unsatisfactory results. Emetine may kill the amoebae embedded in the intestinal submucosa but it does not reach the encysted stage in the lumen. When given by the mouth emetine cannot be tolerated in therapeutic doses. Iodine both in organic and inorganic forms pushed to the limit of tolerance is entirely without effect. Chiniofon (Yatren) is of definite value and emetine bismuth iodide is perhaps the most effective single drug against chronic amoebiasis, but like iodoform it is expensive. Yatren acts best in the form of a retention enema as confirmed in practice in Palestine. The combination of this drug by the mouth and rectum has often resulted in eradication of *E. histolytica* but it is not always well tolerated and the number of relapses is high. Iodoform (0.25 gm. in enteric capsules) has a definite amoebicidal action and has been tried in 60 cases. Though the therapeutic effects are at least as good as those of yatren, untoward results have been observed, such as skin rashes, diarrhoea, vertigo and even collapse.

Novarsenobillon and trypanamide injections are entirely without effect though stovarsol and carbarsone by oral administration are of definite value as adjuncts to other treatments; these are unable themselves to eradicate the infection, but result sometimes in symptomatic relief.

Several methods of treatment are based on the combination of two or more of the drugs already mentioned. There is the E.B.I. and yatren combination. CRAIG and others in U.S.A. prefer yatren and carbarsone. In Palestine it has been customary to administer E.B.I. and yatren in combination, followed by a course of stovarsol or carbarsone.

All combinations have been tried out and the highest percentage of success was obtained by the E.B.I. yatren-carbarsone treatment but it is expensive and entails hospitalization, followed by a considerable period of convalescence.

The author does not consider that we yet possess a practical and efficient treatment for chronic amoebiasis. The matter is further complicated by the fact that immunity to reinfection does not exist. Hence what may appear to be a relapse may be a reinfection.

After a considerable period of clinical experimentation the author evolved a mixture of powdered ipecacuanha and yatrien as follows —

Pulv ipecac 0.15 gm

Yatrien 0.4 gm

The powder is given twice daily in cachets or gelatin capsules 3-4 hours after breakfast and dinner followed by a fast of one hour at least. It is not advisable to permit the patient too much freedom of movement nor to administer the treatment to ambulatory patients. The treatment lasts 12-14 days and may be followed by a short course of carbarzone (2 tablets daily for 6-8 days).

In the majority cysts of *E. histolytica* disappear from the faeces within 8-10 days of treatment. Sometimes active amoebae appear on the sixth or seventh day. This observation is interpreted as suggestive that either the amoebae are unable to encyst or that the cyst wall is dissolved but they eventually disappear.

Symptomatic relief is the rule within the first ten days. Out of 50 cases there has been one relapse only which occurred within one month. 20 were followed up for periods ranging from three months to one year. In all repeated faeces examinations failed to reveal amoebae or cysts. Taking all the difficulties regarding follow up into consideration it is claimed that this treatment is at least as efficacious as any other. It is easy to administer, toxicity and cost are relatively low. Slight diarrhoea is usually noted.

The most important sequelae encountered were chronic appendicitis, chronic haemorrhagic proctitis and post amoebic mucous colitis. Pathologically the appendix shows usually a normal mucosa with one or two islands of superficial ulceration. If it is removed before anti amoebic treatment is given amoebae may usually be found in the ulcers. For some reason the appendix does not show the retrogression of the ulcers observed in the sigmoid after treatment. In haemorrhagic proctitis a diffuse redness of the mucosa of the lower third of the rectum is observed. The real aetiology is not understood. Post amoebic colitis does not differ from mucous colitis or irritable colon. Amoebiasis may be the trigger which initiates colitis in a susceptible individual. Treatment is disappointing and the condition is aggravated by a repeat of the anti amoebic treatment.

P. Manson Bahr

DAS GUPTA, N. C. BANERJEE, P. K. & SEN GUPTA, S. B. Fulminating Types of Giardiasis simulating Asiatic Cholera and Acute Bacillary Dysentery. *J Indian Med Ass.* 1944 Aug. 13 No. 11 317-18.

The authors write that giardia is not only pathogenic but is steadily coming to occupy an important position among the intestinal infections in tropical countries as *Entamoeba histolytica*. From the records of the Khulna District Board Laboratory in India it would appear that the incidence of *E. histolytica* infections is more or less stationary while those due to giardia are increasing to such an extent that they have quadrupled in eight years. It is further noted that like smallpox both the protozoal infections have exacerbations every four years. In some cases the flagellate produces symptoms of a fulminating type resembling Asiatic cholera or acute bacillary dysentery. To illustrate this the authors describe three cases in male subjects aged 8, 33 and 3 years respectively in which violent diarrhoea started suddenly developing in one case into a condition resembling cholera. In the others the stools contained mucus, and in all three red blood corpuscles and pus cells occurred in addition to giardia. In the first case the symptoms had lasted barely 6 hours when dramatic relief followed the administration of 0.03 gm. of atabrin musonate. An hour later there was only one motion and following 4 grains of stovarsol there was recovery next day. In the second case a rapid recovery followed the administration of stovarsol alone while a similar result was obtained in the third case with atabrin

by the mouth. In the comments it is admitted that cases 2 and 3 showed a tendency to spontaneous abatement of symptoms before treatment was started. (It does not appear from the paper that other possible causes for the symptoms were excluded and apart from the presence of *gardia* there is no evidence whatever that this flagellate was actually responsible for the choleraic condition in one case and the dysenteric condition in the others. It also seems doubtful whether the figures presented justify the statements made regarding the increase of the protozoal infection mentioned.

C. M. Weyon

RELAPSING FEVER AND OTHER SPIROCHAETOSSES.

BÖGER A. Die latente Rekurrenzinfektion und das Rekurrenzerheumatoid. [Latent Relapsing Fever Infections with Rheumatoid Manifestations.] *Munch med Woch* 1943 Sept. 24 v 90 No. 38/39 549-52.

The author discusses the well known features of European relapsing fever and then gives clinical details of two cases in which the patients developed rheumatoid manifestations affecting especially the back, shoulders and thighs. Exacerbations of 2 to 5 days duration, accompanied by slight fever occurred at intervals of 6 to 14 days and in some respects the manifestations recalled undulant fever. The nature of these infections was determined by the examination of stained blood films especially thick drops when spirochaetes were found, usually in small numbers. The cases responded to treatment with neosalvarsan.

The author mentions that in South Russia and the Caucasus, where the disease is endemic, many cases of relapsing fever occurred amongst the German troops. Concerning the prevalence of cases showing rheumatoid symptoms 46 were noted during three months including 18 at one station comprising 120 patients.

The method of transmission is said to be usually by the body louse but the author considers that the bed bug may also be a carrier.

The main object of the paper however is to call attention to the rheumatoid manifestations that may accompany latent infections of the disease and the necessity for careful blood examination for spirochaetes in all doubtful cases.

E. Hindle

Nájera Angulo L. Transmisión del *Spirochaeta hispanica* por el método de Sparrow Durand. Transmission of *S. hispanica* by Intra-Nasal Instillation. Reprinted from *Bolet Real Soc Española Historia Natural* 1943 v 41 527-30 [11 refs.]

The author has been able to infect white rats by intranasal instillation of a suspension of *S. hispanica*.

Charles Wilcocks

Comex H. G. Rat Bite Fever. Contributions to its History and War Significance. *Bull History of Med.* Baltimore 1944 July v 16 No. 2, 108-15. [23 refs.]

SENEKJE H. A. The Clinical Manifestations of Leptospirosis in Louisiana. *J Amer Med Ass* 1944 Sept 2 v 128 No. 1 5-10 1 fig [Refs. in footnotes.]

A general account of this disease with special reference to clinical manifestations in Louisiana based on reports of 30 cases at the Charity Hospital New Orleans during the past five years.

The incidence among the inpatients from 1939 to 1943 was one case of leptospirosis to 8 445 general admissions and one case to 1,343 general medical

admissions while in 1943 it was one case to 5 263 general admissions and one to 750 general medical admissions. Two of the patients were infected with *L. canicola*.

The onset of the disease was sudden in two-thirds of the cases and enlargement of the liver and jaundice generally developed five to seven days after the fever but two cases were anicteric. The van den Bergh reaction was direct the prothrombin time was prolonged and the hippuric acid excretion was reduced. In three of the cases the liver was not enlarged although jaundice was present. Splenomegaly was present in three haemorrhagic phenomena in 16 and respiratory symptoms in 12 of the cases. There was electro-cardiographic evidence of cardiac lesions. All the patients showed evidence of varying degrees of pathological changes in the kidneys: five had anuria, 24 albuminuria with casts and blood cells, three glycosuria and 25 leucocytosis. The kidney failure was accompanied by the retention of nitrogenous metabolites in the blood. The duration of the disease was three to six weeks and five of the cases were fatal. Most of the patients had a history of exposure to rats or of coming into contact with water or food contaminated with the excreta of rats and possibly of dogs. Thirty out of 45 suspected cases were confirmed by laboratory methods. In seven cases *Leptospira* was found in the blood; in one it was present in the urine and in another in the cerebrospinal fluid. In two fatal cases the organisms were found in Levaditi-stained sections of organs. In 24 cases diagnosis was established by agglutination reactions: the diagnostic titre ranging from 1:300 to 1:1 000 000. Treatment was symptomatic but one patient received 250 cc. of convalescent whole blood in the fourth week of the disease with no appreciable results.

E Hindle

YAWS

CHAMBERS H. D. Juxta-Articular Nodules. *Arch. Dermat. & Syph.* 1944 Aug. v. 50 No. 2 105-8

Observations on 128 patients with juxta-articular nodules were made while the author was attached to the Jamaica Yaws Commission [this *Bulletin* 1935 v. 32 883-885]. The patients were seen in yaws-endemic areas in rural parts of Jamaica and had no history or signs of syphilis. Although yaws is commoner in males than in females, 91 of these cases were in females. Lesions were found in only nine children (six girls and three boys) under 14 years of age and in only 20 persons under 20 years of age. Tiny nodules may be felt as early as 1-2 years after infection with yaws but they usually develop 15-40 years after infection. In one patient with multiple yaws lesions of the bones, juxta-articular nodules were present close to each affected bone.

Of the 128 patients, 110 gave a history of yaws and 112 had a positive Wassermann reaction while in seven it was negative. The numbers and positions of the nodules are shown in a table: there were 228 nodules of which 95 were near the elbow, 89 near the knee and 17 near the ankle.

The response to specific treatment was definite although slow and long drawn out. Treatment with bismuth subsalicylate (10 per cent. in olive oil) was quite as effective at least as treatment with neocarsphenamine. Small nodules of from one to three years duration may be expected to disappear within six to twelve months.

J. F. Corson

CURI N. Primi casi di pian riscontrati nel Governo dell'Amara. [The First Cases of Yaws in Amara] *Boll. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea) 1943 v. 2 No. 3 45-50 English summary

The author publishes the first three cases of Pian (yaws) diagnosed in the Amara province of Ethiopia

LEPROSY

DE SOUZA ARAUJO H. C. Culturas de bacilos ácido-álcool resistentes isolados de hematófagos infectados em leprosos. Evidências de se tratar do bacilo de Hansen. [Cultivation of Acid-alcohol-fast Bacilli from Bloodsucking Insects fed on Lepers.] *Mem. Inst. Oswaldo Cruz* 1944 Feb v. 40 No. 1 9-31 1 coloured pl. & 40 figs. English summary

Work carried out by Professor de Souza-Araujo must always command respect and that described in this paper may have far-reaching results. The bodies of certain ticks, *Amblyomma cajennense*, *Boophilus microplus* and of the bug *Triatoma infestans* which had been allowed to feed on lepers four days before were triturated in distilled water as a haemolysing agent and inoculated on to Löwenstein's medium. In eight weeks or so signs of growth were observed. A well-reproduced coloured plate shows the culture tubes and stained bacilli. The cultures were pigmented, golden yellow, orange, or carrot yellow and the organisms were acid-alcohol-acetone-fast. They exhibited very marked Brownian movement and gave the impression of actual locomotion. Subculturing in glycerin media yields a film which can be used for antigen employable for skin reactions and consequently the author believes that he has succeeded in cultivating Hansen's bacillus. [See below] *H. Harold Scott.*

DE SOUZA ARAUJO H. C. Preparo de antígenos (Leprolinas Souza Araujo) de culturas de bacilos ácido-álcool resistentes isolados de leprosos. Seu emprego intradérmico comparativamente com o da Leprolina, e subcutâneo ou intravenoso como tentativa terapêutica. [Preparation of De Souza Araujo's Leprolinas.] *Mem. Inst. Oswaldo Cruz* 1943 Dec. 39 No. 3 349-55 5 figs. English summary

In this contribution Professor de Souza Araujo details his method of preparing the antigens from his cultures of acid-alcohol-resistant organisms obtained by allowing certain insects to feed on lepers. These antigens have been used for skin reactions and for comparing these with leprosum reactions [see José MARIANO below]. Of the many cultures he has grown, only four give a film on glycerin broth sufficient to yield a serviceable antigen. On the advice of Dr A. MACHADO of the Oswaldo Cruz Institute the following is the procedure adopted —

1. To 120 cc. of the medium, with a thick deposit and complete rugose film of yellow colour 0.06 cc. of liquefied phenol is added. After vigorous shaking it is placed in the ice-chest for 24 hours.

2. The contents are then transferred to a 600 cc. flask with 50 gm. of sterile porcelain beads and the flask is placed in an electric shaker for ten days and nights by which time the product is a homogeneous, chocolate-coloured milky fluid.

3 A few drops of this are sown on Löwenstein & medium and on 5 per cent glycerin agar and incubated for five days at 37°C to test sterility

4 To the emulsion of this 0.5 per cent phenol is added in a proportion of 10 cc to 100 cc and the product is distributed in 2 cc. ampoules

For comparative tests with lepromin these antigens are injected intracutaneously in doses of 0.2 cc in the front of the arms as related in the following abstract. The author has sent material for trial to various leproseries and leper colonies, 17 altogether five in S Paulo two each in Colombia, Pará, Paraná, Minas Gerais and elsewhere. Tests are also to be undertaken to determine their use therapeutically by injecting the leprolins into resistant lesions.

H. Harold Scott

MARIANO J. Resultados do emprego das leprolinas. Souza-Araujo comparativamente com o da lepromina. [Skin Tests with Leprolins as compared with Lepromin.] Mem Inst Oswaldo Cruz 1944 Feb v 40 No. 1 101-19 1 fig

Tests have been carried out in lepers in the stages mentioned below using leprolins from five cultures from Professor Souza-Araujo (see above abstract) numbered 1 to 5 each injected intradermally three on one arm two on the other injecting 0.2 cc in the sixth place lepromin was injected. The subjects were divided into ten groups according to clinical form and stage. L1 \1 N2 N3 L1N1 L2N2 L1N2 L2N1 L3N1 and L3N2.

The results of the hundreds of tests performed on these patients are presented in a series of Tables. For details those interested must consult the originals. Here we must be content with summarizing them —

1 In 16 nerve cases leprolin 2 was positive in 12 negative in 4 lepromin giving closely similar results, 13 and 3 respectively.

2 In 75 lepromatous cases leprolin 3 (from *Amblostrongia cayennense*) gave a negative in 59 positive in 16 lepromin gave 72 and 3.

3 Of 20 contacts and persons under observation in apparent health the results were again closely similar leprolin 2 gave 12 positive 8 negative lepromin 13 and 7 respectively.

For better comparative estimation it will be advisable to carry out more tests with increasing doses of the leprolins to arrive at a standard product giving the best results and so be of value for prognostic purposes as an evaluation of the defences of the body.

H. Harold Scott

HELMINTHIASIS

KRAKOWER C. HOFFMAN W. A. & AXTMAYER, J. H. Defective Granular Eggshell Formation by *Schistosoma mansoni* in Experimentally Infected Guinea Pigs on a Vitamin C Deficient Diet. J Infect Dis 1944 May-June v 74 No 3 178-83 1 fig

In guineapigs experimentally infected with *Schistosoma mansoni* and kept on a diet deficient in vitamin C the authors found large numbers of eggs of this trematode which showed evidence of disintegration of their shells. In normal guineapigs although tissue reaction may cause deformations (wrinkling fractures thinning) the egg shells remain refractile and homogeneous. The

disintegration of the egg shells was most marked in the eggs in the liver and lungs where at times most of the eggs were so involved. Fertilized eggs with developing miracidia always retained intact shells.

The tissue reaction round the eggs in the guinea-pigs on scorbutic diet did not differ in any major way from that seen in controls, except that eosinophil response was less and there were haemorrhages.

The authors then enquired whether humoral or intracellular reactions due to deficiency of vitamin C might act upon a less defective or normal egg shell and cause its disintegration. Eggs were obtained free from all tissues by a method of sterile sedimentation which is described, and these were injected subcutaneously into marked areas of guinea-pigs on a scorbutic diet. One lot was given intratracheally because most of the disintegrated eggs had been found in the liver and lungs. In several such trials granular disintegrated eggs were never found. From the second to the third month after injection of these eggs into guinea-pigs protected against scurvy fewer and fewer eggs were found and the authors suggest that they were absorbed or dispersed and greatly reduced in volume by fibrosis and reorientation of the organized tissues (cf. KRAKOWER HOFFMAN and AXTMAYER this Bulletin 1943 v 40 823).

Deficiency of vitamin C thus did not interfere with the development of *Schistosoma* nor to a certain extent with fertilization or development of the miracidia except when bacteremia in the hosts infected the parasites.

There was no reason to suppose that any other vitamin was concerned in the changes observed.

G. LaPage

VAZZOTTI L. Presencia de huevecillos de *Tecnia* en la región perianal (Eggs of *Tecnia* on the Perianal Skin.) *Rev. Inst. Salubridad y Enfermedades Trop. Mexico* 1944 June v 5, No 2 153-5 English summary

Sixteen patients harboring *Tecnia* were examined by Graham's method during several days. Out of 63 examinations 44 (70%) were positive which show that the eggs were present on the skin of the perianal region of these patients.

RITTER C. Solitary and multiple Muskeleystercysten. [Single and Multiple Cysticercus in Muscle.] *Dtsch. Ztschr. f. Chirurgie* 1943 June 22 v 257 No. 9-12 684-83 1 fig.

Two cases of human infestation with cysts of tape worm are described and the subject is discussed in considerable detail. In one case, in a 12 year-old girl a cyst of about the size of a cherry stone was removed from the right rectus abdominis muscle. It was found embedded in the muscle without intervening connective tissue. *Mikroskopische examination showed it to be Cysticercus cellulosae*. The second case was in a middle-aged man who had broken his right femur 3 years before and who complained of such severe and prolonged pain that walking and working were very difficult. By interrogation and examination it was found that the pains were not confined to the right leg but were present all over the body. X-rays showed that the fracture was firmly united and also showed, unexpectedly, the presence of numerous calcified cysticerci, widely distributed in the muscles of the body and especially numerous in the region of the adductor muscles of the right thigh.

The author discusses the various views on how man may become infected, the pathology, symptomatology, diagnosis, prognosis and treatment, quoting the findings of numerous workers. With regard to treatment solitary cysts are removed by operation. For multiple cysts there is no treatment.

J. F. Corson.

SMIRNOV G G On the Efficiency of Cutaneous Infection with Hookworm Larvae. *C R (Doklady) Acad Sci de URSS* 1944 v 42 No 1 46-8 [In English]

Continuing his studies on the rate of penetration of the skin of the hamster (*Mesocricetus brandti*) by larvae of *Ancylostoma duodenale* and *Necator americanus* the author describes the method used. Entomological test tubes measuring 12 by 2 cm were filled to the brim with water and put in a water bath at 40°C. Each was covered with a small piece of the freshly removed abdominal skin of the hamster all the pieces being taken from hamsters of the same age. The skin was stretched and fixed in place by a rubber ring. Counted larvae generally between 500 and 600 were put on the skin with a pipette. After 15 30 45 and 60 minutes the number of larvae left on the skin was counted and also the number in the water beneath. The experiments were done in July at Tbilisi Tropical Institute and the laboratory temperature was 28-34°C.

The author discusses the thigmotactic and thermotactic responses of the larvae and their alternating periods of rest and activity and the bearing of these upon the varying rate of their penetration of the skin. G. Lapage

PALMER E D A Consideration of certain Problems presented by a Case of Strongyloidiasis. *Amer J Trop Med* 1944 July v 24 No 4 249-54 [25 refs.]

The author describes a case of infestation with *Strongyloides stercoralis* complicated by disseminated tuberculosis. The patient was a Polish junk yard worker aged 63 admitted to a hospital in Rochester N.Y. complaining chiefly of stomach trouble and diarrhoea which began two weeks previously when the patient also had sharp non radiating periumbilical pain. He was acutely ill and his condition is described in detail. There was no eosinophilia and the number of leucocytes varied throughout the illness around the lower normal limit. Several direct faecal examinations failed to reveal any protozoa or nematode larvae or eggs but on the sixth day examination by the zinc sulphate centrifugal floatation method revealed many larvae of *Strongyloides stercoralis*. On the seventh day the patient was started on a course of 0.06 gm gentian violet in enteric-coated tablets three times a day before meals on the twelfth day he was also given 0.1 gm gentian violet intravenously in a 0.5 per cent. solution. On the ninth day when gentian violet first appeared in the stools even direct stool examination revealed abundant larvae of *S. stercoralis* but by the thirteenth day none was found even by concentration methods. The author emphasizes the need for concentration methods for the faecal examinations. The patient died on the fifteenth day by which time he had had a total of 1.56 gm. of gentian violet by the mouth and 0.1 gm intravenously.

At autopsy no evidence of pulmonary or intestinal infestation with *Strongyloides* was found there were no adult or larval worms and no eosinophil tissue reaction. The author thinks that the gentian violet had eliminated the infestation [cf v ENGEL this *Bulletin* 1945 v 42, 49].

The author concludes that the infestation was a chronic one and that it could have originated either in Poland or in Rochester. The patient had lived 33 years in Poland and 30 years in Rochester. If the infestation had been acquired in Poland it must have persisted by auto-infection or hyperinfection for 30 years. Two records of infestations lasting 20 years are recorded viz SCHÄFER and LODENKÄMPER, *Die Med Welt* 1935 v 9 1241 and BODOV [this *Bulletin* 1942, v 39 101]. But the patient might have been infested by his habit of lying on the ground in the Rochester junk yard although there was no evidence

of *Strongyloides* infestation in seven of his co-workers. The author reviews the literature of strongyloidiasis in the United States and concludes that further study is needed to determine the northern limit of the natural distribution of this parasite. Three cases of this infestation have been recorded in Rochester during the last three years. The author discusses the pulmonary lesions which the migrating larvae of *S. stercoralis* may cause [cf. SILVEIRA, this Bulletin 1945 v 42, 46] and also the relation of this infestation to the generalized signs of tuberculosis present. He suggests that the recent migration of a significant number of *Strongyloides* larvae through the lungs may have been associated with the development of the fulminating disseminated tuberculosis from an old inactive pulmonary process. Clinical examination had revealed an extensive old infection with fibrotic change and calcified lesions. tuberculous broncho-pneumonia was found at autopsy, and sputum, available for the first time two days before the patient's death, contained tubercle bacilli. Nine years previously the patient had at the same hospital undergone an ileotransverse colostomy. Examined then for acute intestinal perforation, much cloudy fluid was found in the abdominal and pelvic cavities and also a large very hard mass grossly resembling a carcinoma, involving the ascending colon and hepatic flexure with hard nodes throughout the mesentery and an adherent omentum but no perforation. The hard tissue was found to be organizing connective tissue with many round cells and fewer polymorphs but there was no evidence of tuberculosis or worms in it. The patient had apparently remained well since this operation. The author quotes the statement of BLACKIE (*J Amer Med Ass* 1939 v 112, 832) that he had not seen intestinal disease which could be with certainty ascribed to *Strongyloides* infestation. Palmer considers that the patient under consideration is a case in point. He comes to no conclusion about the possible part played by *Strongyloides* in the causation of this hard mass in the bowel, but quotes the work of BLACKLOCK and ADLER (*Ann Trop Med* 1922, v 16, 283) on thickening of the jejunum of a chimpanzee due to *Strongyloides* and that of PRICE and DICKINSON (*J Parasitology* 1929 v 18, 104) on multiple adenomata of the colon of a cat caused by an apparently new species of *Strongyloides*.
G Lapage

CULBERTSON J T & ROSE H M Chemotherapy of Filariasis in the Cotton Rat by Administration of Neostam and of Neostibosan. *J Pharm. & Exper Therap* 1944 June v 81 No 2 189-96 3 figs

Two antunomials drugs stibamine glucoide (neostam Burroughs Wellcome & Co.) and metachlor paracetylanunophenyl stibate of sodium (neostibosan) were found to be particularly effective against the filarial worm, *Litomosoides carinii* in cotton rats (*Sigmodon hispidus*). The adult worms were killed in the pleural cavity and the microfilariae disappeared from the peripheral blood. Various experiments were made and the results are shown in tables (some have been previously reported see this Bulletin 1944 v 41 772). The drugs were given by intramuscular injection instead of intravenously, because the rats were difficult to handle. The dose of neostam was 40-60 mgm. for rats weighing 100-150 gm. In one experiment with 4 rats a single dose of 40 mgm. killed the adult worms in all the rats, but a few microfilariae were still present in the blood of one when it was killed after 76 days. Neostibosan was given in two courses of injections. 40 mgm. every day or two for 11 doses then an interval of 26 days then 80 mgm. every few days for 8 doses. The effects were similar to those produced by neostam.

Both drugs had also a powerful action *in vitro* on the adult worms. concentrations of neostam of 1 to 5 mgm. per cent. killed the worms in four days at 37°C and one of 50 mgm. per cent. killed them within 24 hours. J F Corson

LATIENDA R. I. & CARPANELLI J. B. Appendicitis & *Oxyuris* [Appendicitis and *Oxyuris*] *Rev. Asoc. Med. Argentina* 1944 Aug 15 v. 58 No. 539 627-31 6 figs [33 refs]

The authors describe eight cases in which *Oxyuris* was found in appendices surgically removed. The diagnosis of three cases was acute appendicitis of one subacute appendicitis of one chronic appendicitis and of one strangulated hernia. In one case *Oxyuris* was present in the wall of the appendix in all the others the oxyurids were in its lumen. The histological picture was not typical. All the cases showed fibropomatosis of the appendicular submucosa with many eosinophils and moderate reaction of the appendicular lymphatic tissue. The authors agree with other authors that the clinical picture presented in many cases not justified by the lesions found. *Oxyuris* commonly occurs in the appendix without causing any symptoms. Appendicular inflammation may occur in any individual harbouring *Oxyuris*. The blood eosinophil count may be normal or low. Antiparasitic treatment should be given. Faecal examination should be done but it may be negative because the eggs do not always appear in the faeces. Some of the literature dealing with the incidence of *Oxyuris* and the question whether it can cause appendicitis is discussed. (See also RECTOR this *Bulletin* 1943 v. 40 927) G. Lapage

PIROT R. & BOURGAIN M. *Moniliformis moniliformis* rencontré à Toulon dans l'intestin des murides des navires de guerre. *Moniliformis moniliformis* found at Toulon in the Intestine of Rats from Battleships. *Inr. Para. Humaine et Comparée* 1942-1943 v. 19 Nos. 4-5-6 124-8 4 figs

The author found 50 specimens of this species which belongs to the *Cl. Acanthocephala* in 9 rats (*Mus al. vandrinus* M. *rattus* and M. *d. cumanus*) taken from one battleship at Toulon. There was a minimum of 5 worms per rat. The description of the worm does not differ from that given in text books but the following measurements may be recorded here: length of the worm 4 to 14 cm. the diameter can reach 3 mm. average length of the female when full of eggs 13 cm. and of the male 5-7 cm. Average length of the proboscis male 448 microns female 481 microns. Average length of the proboscis 3.15 to 4 mm. female 7.55 to 8 mm. Hooks of both sexes 19-20 microns long. Eggs 107 to 118 microns (average 114 microns) long by 57 microns across the widest part of their elliptical shape. Three membranes cover the spined embryo in the egg. Embryo 80 to 91.2 microns long by 25 to 30 broad. For more detailed measurements the paper should be consulted.

The authors are studying the distribution of this species in the Toulon region in the rats and in the intermediate host (cockroach). CRAIG and FAIST (*Clinical Parasitology* 3rd ed. 1943 p. 467) state that apparently authenticated cases of human infection have been reported from Italy, the Sudan and British Honduras.] G. Lapage

DEFICIENCY DISEASES

WILKINSON P. B. Deficiency Diseases in Hong-Kong. *Lancet* 1944 v. 635-8

Today poverty is probably more widespread and more devastating effects in China than anywhere else in the world. The diets are defective in northern and southern China in the former calcium vitamins A, B

probably D are deficient in the latter first-class protein, vitamins A, B₁, B₂, and possibly D. Food habits of these peoples are also factors in inducing deficiencies and attention is called to the well-known difficulty of attempting to effect any change. Night blindness, hyperkeratosis infantile and adult rickets, scurvy, pellagra and beriberi are all found in northern China, while in southern China

beriberi abounds and coexists with pellagra and certain other syndromes probably caused by lack of part of the B complex. Scurvy, rickets and eye changes found in vitamin A deficiency are not common. The increase in beriberi is reflected in the admission figures with deaths for Hong Kong: 1937—2,869 (928); 1938—5,373 (1,885); 1939—8,518 (2,061); 1940—15,129 (4,300). Latent and minor beriberi is very prevalent though not shown in these figures. On the other hand fulminant cardiac beriberi is uncommon in S. China and Hong Kong. Emphasis is laid on the necessity of high dosage in these cases of acute cardiac beriberi—60 mgm. thiamin intravenously 3 times in the first 24 hours and thereafter once daily until full cardiac response is obtained.

Pellagra broke out suddenly in April 1940, nearly 1,000 cases occurred in one province in the next four months, with 50 per cent. mortality among the population which was existing on a diet of rice, salt fish and vegetables. It is stated "No signs of organic involvement of the nervous system were seen but nervous symptoms were prominent." It is interesting that 253 patients out of these 420 [cases recorded by HUI & CHENG this *Bulletin* 1944 v 41: 419] showed signs of beriberi. Only two cases of pellagra since pellagra were seen but two other syndromes deserve mention here because they are probably pellagrous if indeed they are not just unusual types of pellagra itself. Of the first, the outstanding signs and symptoms were angular stomatitis, glossitis [of a dusky bluish red], scrotal eczema, giddiness and weakness of the legs.

Occasionally one of these patients would complain of dimness of vision but this was rare. The signs of cord involvement were present in a considerable percentage of the men. These cases responded to marmite and are recognized as identical with those described by LADDON and PALLISTER in 1935 [*Bulletin of Hygiene* 1935 v 10: 733]. The authors add "it is tempting to speculate on the possibility of its being a pure arboflavinosis [as others have already done]."

The other pellagra-like syndrome was first noted in June 1940 when classical pellagra was rampant [WILKINSON & KING this *Bulletin* 1944 v 41: 667]. Its outstanding feature was a rapidly oncoming painless reduction of visual acuity associated with a well-marked concentric constriction of the fields of vision. Common associated symptoms were giddiness, acroparaesthesiae, palpitation and weakness and puffiness of the limbs, sore tongue and angular stomatitis, but no dermatitis. The second syndrome apparently responded to riboflavin or nicotinic acid. Scurvy and rickets were rarely seen.

Xerophthalmia occurred during 1939-40 but was not common. Bitot's spots on the other hand, were quite common, associated often with lichen planus [sic] most commonly on the arms, forearms, thighs and popliteal fossae. This eruption was a follicular hyperkeratosis associated with dryness of the skin, but no pustulation or pigmentation and was commonest in the 15-25 years age group.

H. S. STAMMIS.

FASAL, P. Clinical Manifestations of Vitamin Deficiencies as observed in the Federated Malay States. *Arch. Dermat. & Syph.* 1944 Sept v 50 No. 3: 160-68 6 figs. [Refs. in footnotes.]

During the years 1939-41 nutritional surveys were carried out, organized by Dr A. NEAVE KINGSBURY, Director of the Institute for Medical Research, Kuala Lumpur. Dr FASAL assisted in carrying out the work (*vide Ann. Med. Reports*). Four thousand Malay and 6,000 Indian children and young adults

were examined. The Malay children were seen at some 36 schools with a population of from 30-300 the Tamils on some 60 plantations where their parents worked. The results in tabular form were as follows —

	Total examined	Phrynoderma	Bitot's spots	Angular stomatitis
		Per cent	Per cent	Per cent.
Malay	1 482	2.6	2.9	4.7
Tamil (Indian)	3 657	25.6	8.4	22.2

In mild cases of phrynoderma the changes in the skin resembled those of ichthyosis except that the palms and soles were not affected. The lesions in the severer cases both in character and distribution resembled those already described many times by other writers—follicular keratosis. The greater incidence of this condition in the Tamils as compared with the Malays makes an interesting contrast the same being true for Bitot's spots and angular stomatitis all easily accounted for by the pooriness of the diet of the Indian compared with that of the Malay.

With vitamin A the skin lesions improved rapidly the preparation used being locally produced red palm oil with a vitamin A equivalent of 1 000 i.u. per cc. given by mouth or applied locally. As a control it was shown that coconut oil (which contains no vitamin A and no carotene) had no effect. There are some cases however which do not improve unless the intake of protein is increased and B complex given.

The angular stomatitis cleared up with B complex or riboflavin. There are some most excellent photographs of the dermatosis and of a section of the lesion of Bitot's spots and angular stomatitis.

H. S. STANNUS

FEHILY Lydia Human-Milk Intoxication due to B₁ Avitaminosis *Brit Med J*
1944 Nov 4 590-92. (20 refs.)

In this paper Dr Fehily returns again to the subject which she has been studying for some years past and the points she brings forward help greatly in elucidating an obscure condition which has gone by the name infantile beri beri. She adduces evidence to show that this name is not a good indication of the true state of affairs the condition is rather an intoxication (sometimes acute at others chronic) of infants by a poison in the breast milk of mothers in a state of B₁ avitaminosis [see this *Bulletin* 1941 v 38 282 1942 v 39 332 784 1944 v 41 142]. One of these poisons perhaps the chief is methylglyoxal (pyruvic aldehyde). The term breast milk intoxication suggested by ITO in 1911 or human milk intoxication suggested by the author is therefore preferable to infantile beri beri. The symptoms are fairly definite vomiting abdominal pain diarrhoea and meteorism perhaps with stiffness of the neck and limbs and convulsions coming on soon after breast feeding such may be fatal the less acute show oedema oliguria aphonia enlarged liver dilated heart and marasmus. At the beginning of the intoxication the infants are often fat flabby and restless and many suffer from bronchitis and bronchopneumonia. The overfed suffer most because they ingest more of the poison.

During 1929 as many as 18 per cent. of infants under the author's observation at a welfare centre in Hong Kong showed signs of this milk intoxication and 25 per cent. of the mothers had early symptoms of avitaminosis B₁. At autopsy little may be found some degree of oedema of brain larvae and lungs & erosions

effusions and enlargement of the right side of the heart but at times nothing sufficient to account for death which may then be ascribed to overlaying asphyxiation from charcoal fumes or poisoning by native medicines. Women in Hong Kong often live on the borders of avitaminosis B₂ from eating highly polished rice and when they become pregnant the danger becomes greater owing to increased intake.

These cases are not however confined to Hong Kong or the Far East they have been reported from Palestine Rumania and America and probably occur elsewhere wherever BBS [intermediary metabolites known as bisulphite-binding substances] are increased in the human body and this may occur not only in B₂ avitaminosis but also in other conditions of toxæmia such as diabetes uræmia and epidemic dropsy, for example. [A considerable part of the information in this article was covered by STANNUS in a paper published in the *Lancet* in June 1942. Stannus deals however more with the chemical aspect Dr Fehily with the clinical as met with in her experience in Hong Kong. In her list of references Dr Fehily omits to mention the paper by Stannus]

H Harold Scott

BOYKARD Augusta Supplement to Breast Feed. [Correspondence.] *Brit Med J* 1944 Nov 23 707-8 Summary also appears in *Bulletin of Hygiene*

The paper by FETILY [above] has prompted the author to call attention to the effects on the child of protein deficiency in the mother's milk a condition that is becoming increasingly common nowadays under rationing conditions. This qualitative change is partly attributable in the author's opinion to the effect on the mother's diet of such "food fads" as refusal of fish and cheese and sharing the punt of milk it may also be associated with imperfect recovery from childbirth. Test feeds may show that the milk is adequate or even abundant in quantity. In the welfare clinics attended by the author about one new baby in six suffers from the effects of this deficiency in the mother's milk. The child feeds voraciously but is not satisfied it is restless, irritable and sleeps badly and gains little if any weight. The stools are dark green and contain curd and sometimes slime.

An immediate cure is brought about by supplementing the mother's milk with small amounts of cow's milk for a child a month old one tablespoonful is given thrice daily and at no suckling age is it necessary to give more than 4 tablespoonfuls four times a day. Within a week the child may gain 8-12 oz in weight the stools become normal and the other symptoms disappear. [The author gives no figures of milk analyses in such cases.]

J F Corson

TOMASSI G Studi sulla vitamina C in Eritrea. Nota 4 Considerazioni cliniche sullo scorbuto in Eritrea. [Studies on Vitamin C in Eritrea 4 Clinical Scurvy. *Boll Soc Ital di Med e Igiene Trop* (Sez. Eritrea) 1943 v 2 No. 1 87-90 English summary (8 lines)]

The natives in Africa rarely suffer from scurvy but when they are recruited by Europeans for work and their diet is changed or the food not properly prepared being overcooked for example, signs of scurvy may make their appearance. In 1940-42 the author observed about 140 cases. The patients were dabby and undernourished drowsy with fleeting rheumatic pains swollen gums were present in about 70 per cent. and in some the teeth were falling out occasionally petechial haemorrhages and even larger haemorrhagic effusions were seen in the calves legs, feet and trunk rarely epistaxis and melaena. Thirty per cent. had hemeralopia and 80 per cent. follicular keratitis, signs of avitaminosis

A The symptoms cleared up in a fortnight on treatment with the appropriate vitamins. The natives habitually use red pepper in quantity and the author believes that this in great part accounts for their freedom from scurvy under natural conditions.

H Harold Scott

HAEMATOLOGY

MCGAVACK T H & GERMAN W M Sicklemlia in the Black Carib Indian
Amer J Med Sci 1944 Sept. v 208 No 3 350-55 1 fig [28 refs]

In wet unstained preparations the red blood cells of 24 of 300 Carib Indians of Honduras Central America showed the sickling phenomenon within a period of 24 hours. The sex and age incidence are noted. None of the individuals who showed sickling could be proved to have had active episodes of sickle cell anemia at any period of life. The significance of the findings is discussed particularly in relation to the hereditary racial nature of the disease and the sickling trait and the environmental influences which may play a part in precipitating the crises

SEGURA G RADICE J C, DOWEN L & GIUSTI C L Estudio anatomico-patologico del primer caso argentino de anemia falciforme [The First Case of Sickle Cell Anemia in Argentina] *Rev Asoc Med Argentina* 1944 Sept. 15 v 58 No 541 731-9 9 figs. [42 refs.]

BRUGSCH H G & GILL Dorothy Polyarthritls in Sickle-Cell Anemia *New England J of Med* 1944 Aug 24 v 231 No 8 291-2

Four cases of sickle-cell anemia are discussed in which the diagnosis was obscured by the presence of polyarthritls and heart murmurs simulating rheumatic fever

MAJUMDER, D N & DAS GUPTA C. R. Haematological Studies in *Silenus* (*Macacus*) *rhesus* Part I. The Blood Picture of the Normal Monkey *Indian J Med Res* 1944 May v 32, No 1 101-4 8 graphs.

VENOMS AND ANTIVENENES

SERGEANT Et. L action du serum antiscorpionique est renforcée quand on injecte en même temps de l'eau salée [The Action of Scorpion Antivenene is Reinforced by Simultaneous Injection of Physiological Saline.] *Arch Inst. Pasteur d Algérie* 1943 Mar v 21 No 1 24-7

Previous work has shown that injection of physiological saline alone in animals injected with fatal doses of viper or scorpion venom will prevent death in 27.4 per cent. The author records one human case of scorpion sting in which subcutaneous injection of 100 cc. apparently led to recovery although the patient was *in extremis*. In another case this treatment was ineffective. He also quotes success in four of five cases treated with scorpion antivenene (20-40 cc.) and with physiological saline administered separately in subcutaneous doses of 150-500 cc. or (in one) an intravenous dose of 10 cc. antivenene diluted with 10 cc. saline. In 109 mice treated after injection of a fatal dose

of venom with serum alone, 78.8 per cent. recovered in 105 treated with serum and saline 85.7 per cent. recovered. The advice is therefore given that, in addition to antivenene saline can with benefit, be used in human cases.

Charles Wilcocks

DERMATOLOGY AND FUNGUS DISEASES

BYRNE E. A. J. with the assistance of J. H. CROXON. Bactericidal and Fungicidal Action of Organic Mercurials with special reference to the Dermatomycoses. *Indian Med Gaz* 1944 Aug v 79 No 8 357-61 [12 refs.] Also in *Indian Physician* 1944 Sept. v 3 No 9 277-85 [14 refs.]

After discussing the history chemical and physical properties of these substances the authors describe the three types of base in which they incorporated either phenyl mercuric chloride (P.M.C.) or phenyl mercuric acetate (P.M.A.) The following formulae are given for the chloride —

Phenyl mercuric chloride	0.20 per cent.
Eucern	3 parts
Distilled water	5 parts
or	
0.5 per cent. of the salt impregnated on Calamine B.P.	gr 15
Glycerin	m. 30
Zinc oxide	gr 30
Water	to oz. 1
The acetate is used as—	
Phenyl mercuric acetate	0.125 per cent.
Eucern	3 parts
Distilled water	5 parts
or	
Phenyl mercuric acetate	0.05 per cent.
Sterile distilled water	oz. 1

Full dispensing details are given in each case. [The percentages of the organic mercurials in the formulae presumably represent final concentrations in the preparations.]

Cases of ringworm of the trunk and limbs (115 in number) and those of tinea cruris (62) were apparently cured after only one application of either 0.20 per cent. P.M.C. or 0.125 per cent. P.M.A. for three to four hours. Early examples of tinea pedis (20) required two to five days. It is stressed that older keratotic and fissuring cases do not react so well and indeed usually show later relapse. "Jungle sores" healed after preliminary application of 1/2,000 P.M.A. with subsequent use of elastoplast.

Sydney Thomson

GONZÁLEZ OCHOA, A. & RUILOBA, J. Acción del propionato de sodio in vitro sobre *Actinomyces viscosus* y *Cephalosporium* sp. Ensayo terapéutico en micetomas producidos por estos hongos. [In vitro and Therapeutic Trials of Sodium Propionate against *Actinomyces viscosus* and *Cephalosporium* sp.] *Rev Inst Salubridad y Enfermedades Trop. Mexico*, 1944 June v 5 No. 2, 83-6 2 charts. English summary.

The therapeutic trials were unsuccessful.

DE ALMEIDA PRADO A. Blastomicose do pulmão e das capsulas suprarenais. Síndrome de cardíaco negro [Blastomycosis of the Lungs and Suprarenals Syndrome of Cardíaco Negro] *Rev Asoc Med Argentina* 1944 Sept '90 v 58 No 542 789-93 6 figs [11 refs]

Cardíaco negro is the name given to the condition in which the patient has almost a black appearance owing to intense cyanosis such as occurs in congenital pulmonary stenosis or in acquired stenosis of the pulmonary arteries usually syphilitic in nature. *Ayerza's* disease or better *Ayerza's* syndrome. The patient in this case was a Portuguese 50 years of age, who was admitted with orthopnoea and intense dyspnoea, oedema of limbs and face, an intractable cough, widespread cyanosis, intense venous engorgement, the heart was enlarged, globar in outline, the lungs showed basal oedema, liver enlarged to three fingers' breadth below the costal margin, ascites present and abdominal wall oedematous. The patient died the same night in a heart attack. Autopsy revealed a healed mycotic scar on the nasal septum (the patient mentioned that he had had this trouble two years before coming to hospital), a generalized pulmonary fibrosis with foci of hepatization, bullae and emphysema, and necrotic nodules, lemon yellow in colour and varying in size from millet to half a grape. The coronary vessels were thickened and patchy with atheroma, the pleurae were thickened and on section showed irregular gumma-like nodules. The suprarenal were enlarged with nodules like those in the lungs.

The author adds remarks on blastomycosis in general. He divides it into three groups: (1) *Cryptococcus dermatitidis*, the mycodermis of Gilchrist and Stokes; (2) Coccidioidal granuloma of Gilchrist and Rixford, caused by *Coccidioides immitis*; (3) Paracoccidioidal granuloma due to *Paracoccidioides cerebri* forms or *P. brasiliensis*. He thinks the present case belongs to this third group. [See this *Bulletin* 1928 v 25 32-746 1938 v 35 924 1941 v 38 94.]

H. Harold Scott

ASCHER L. Two Cases of Pulmonary Blastomycosis in Brothers. *Harefuah* Jerusalem. 1944 Oct 1 v 27 No 7 [In Hebrew 124-5 English summary 125]

ZOZAYA J. VARELA G. & CASTRO ESTRADA S. Tratamiento del pinto con penicilina (Nota preliminar) [Treatment of Pinto with Penicillin] *Rev Inst Salubridad y Enfermedades Trop* Mexico 1944 June v 5 No 2 87-9 English summary

Penicillin applied to a patient with Pinto caused the disappearance of *Treponema carateum* from the skin 8 hours after the administration of 50 000 Oxford units.

HEAT STROKE AND ALLIED CONDITIONS

LADELL W. S. S. WATERLOW J. C. & HUDSON M. F. Desert Climate. Physiological and Clinical Observations. *Lancet* 1944 Oct 14 & 21 491-7 527-31 7 figs [20 refs]

1. During the summer of 1943 observations were made in a desert climate on fit soldiers and on cases of effects of heat admitted to a military hospital.
2. All the fit men observed lost some weight in the hot weather. The loss was greatest in those who had the highest chloride concentrations in their

sweat. It is suggested that this loss was due to a minor degree of salt-deficiency dehydration. Calculations based on the measured rate of sweating and the estimated salt intake indicated that subjects with a high concentration of chloride in their sweat (i.e. above 0.3 per cent. NaCl) may not always have been in salt balance. Evidence of a salt-deficiency dehydration was provided by the following findings: low urine output in spite of a high water intake; low urinary chloride output (less than 2 g. a day in some cases); and raised blood urea. No changes were found in the haemoglobin or in the blood and plasma chlorides. Blood-pressure fell as the weather grew hotter but there was no evidence of cardiovascular inefficiency.

3. Twelve cases of hyperpyrexia are described: these conformed to previous descriptions. The onset was acute with absence of sweating and loss of consciousness. These cases all went through a phase of apparent negative water balance: they excreted large quantities of dilute urine at a time when they were drinking very little. During this phase the chloride content of the blood was diminished. These findings support the view that hyperpyrexia is accompanied by superhydration.

"4. Two distinct types of heat exhaustion were seen: these have been designated types I and II.

5. Cases of heat exhaustion type I were seen mainly in the first half of the summer and at the peaks of external temperature. Vomiting and cramps were common in these patients. On admission the patients were pale, collapsed and sweating profusely. The blood-pressure was occasionally low but the most consistent abnormality was a reduction in pulse-pressure: on standing the blood-pressure fell and syncope occurred. Chemically heat exhaustion type I was a salt-deficiency dehydration: plasma and whole-blood chlorides were grossly diminished, haemoglobin and plasma protein were raised, blood-urea was very high, extracellular fluid and plasma volumes were diminished, and the urine was scanty of high specific gravity and almost free from chloride.

"Treatment of these patients consisted in replacement of salt and water. In severe cases intravenous saline was given with excellent results. The patients gained weight rapidly, indicating retention of water and salt. There is evidence that type I heat exhaustion occurs in persons who habitually secrete sweat containing a much higher concentration of chloride than the average: their salt intake is inadequate at high rates of sweating and they become salt-deficient. Prevention of these cases might be achieved by increasing the salt intake of all men but this would probably be impracticable. Potential cases could be picked out and treated before they became casualties by following the body weights and the urinary chloride (by some simple test) of all men exposed to risk. Any man who is consistently losing weight and is excreting a concentrated urine with low or absent chloride should be regarded as a potential case and given extra salt.

"6. Cases of heat exhaustion type II were seen only in the second half of the summer among men who had already come through the hottest weather unscathed. Clinically they were characterised by defective sweating and polyuria: the skin was always more or less severely affected by prickly heat in the healing and desquamating stage. Vomiting, cramps and cardiovascular abnormalities were not present. Chemically these cases were salt-deficient, but not so grossly as those of type I and they were not dehydrated. During convalescence they were found to secrete a sweat with a high concentration of chloride but it is not believed that this was habitual.

"The general picture suggests a breakdown of the defence mechanism of the body against heat. Signs of a similar breakdown were found in some of the fit men observed, in that during the second half of the summer their sweat was richer in chloride than it had been during the first half.

The incidence of heat exhaustion type II could probably be reduced if men—particularly those suffering from severe prickly heat—were given a break of a few days in a cooler climate after 8 weeks' continuous exposure to extreme desert conditions.

MACQUAIDE D H G Congenital Absence of Sweat Glands *Lancet* 1941
Oct. 21 531-2.

The term hereditary ectodermal dysplasia of the anidrotic type was suggested by WEECH (*Amer J Dis Children* 1929 v 37 760) for a condition which has the following main features: total absence of sweat glands and occasionally of subcutaneous glands; dental dysplasia; atrophic rhinitis and depressed nasal bridge; thick protrusive lips; prominent supraorbital ridges; growth of fine scanty lanugo hair; a dry smooth thin skin with frequent papular eruptions especially on the face and the back of the neck and shoulders.

The author describes two cases both in young almen which presented some of these defects including inability to sweat when tested by being placed wrapped in a blanket under a heat cradle. In one patient a biopsy of the skin showed complete absence of sweat glands. Both patients felt discomfort in hot weather and used to dip their hands in cold water to relieve it. Both had scanty hair on the head and body; rhinitis; deficient dentition and protrusive lips. One had never shed tears but in the other lachrymation was normal. X rays showed enlarged nasal fossae; small and absent frontal sinuses respectively; and no unerupted teeth. Intelligence was above the average in both. There was no evidence of ectodermal defects in other members of either family.

Both were considered to be permanently unfit for service in the tropics

J I Corson

HENSCHEL A TAYLOR H L BROZFK J NICKELSEN O & KEYS A Vitamin C and Ability to Work in Hot Environments. *Amer J Trop Med* 1944
July v 24 No 4 259-65 [22 refs]

This work unites two lines of research that have been pursued in recent years at the University of Minnesota—on the results of exposure to heat and on the concentration of vitamins in sweat. Several authors have recently claimed that extra amounts of vitamin C are required at high environmental temperatures particularly when physical work is done. The experiments described below were undertaken to test this view.

Forty-four men were exposed to dry heat (112°-122° F by day 85°-90° F by night with a relative humidity of about 30 per cent.) for periods of up to 3½ days. The diet which was rigidly controlled contained 20-40 mgm. of vitamin C daily. Half the men were given a daily supplement of 500 mgm. ascorbic acid. The subjects worked for two hours each day on a treadmill at an oxygen consumption of about seven times basal. Measurements were made of pulse rate, Crampton score, rectal temperature, rate of sweating, water intake, uric acid output and weight loss. In some experiments strength of grip and of back lift was measured with dynamometers and psychometric functions were tested by coordination tests and measurements of flicker fusion frequency. The concentration of ascorbic acid was estimated in urine, plasma and sweat.

No statistically significant difference between the high-C and low-C groups was found in any of the variables measured except in the ascorbic acid content of plasma and of urine. The average ascorbic acid concentration in the sweat was the same in the two groups—0.08 mgm per 100 ml. In one experiment half the subjects were put on a low chloride intake of 6 to 8 gm. daily. Of 13 men in this group six developed signs of heat exhaustion. Three of these were in the low-C and three in the high-C group.

to concentrate the resistance to infection, especially of the respiratory tract, is reduced. The disease is said to have no connexion whatever with heat stroke or heat prostration

John W. D. Negro

GELFAND M. The Haemorrhagic Bullae in Onyala. *Clin Proc Cape Town* 1944 July-Aug. v 3 No 8 255-9

One of the characteristic features of onyala is the presence of haemorrhagic bullae on the buccal and lingual mucosa. These may be many or few and the question arises, if there are very few say one only, would the fact rule out the diagnosis of onyala? The answer would surely be negative. One is reminded of Abraham pleading on behalf of Sodom and Gomorrah by going, as the author does, even one step further. Peradventure there be none found there, then we should probably agree that if the other symptoms were present—haemorrhages elsewhere, petechiae, thrombocytopenia, etc.—the diagnosis of onyala would still hold good, for if the patient does not die it is not possible to rule out haemorrhagic bullae in the viscera. So here the author quotes three cases, two of them at the same time in one family, girls of two and five years. The former was bleeding from nose, mouth and vagina and had haemorrhagic bullae on the tongue, in fact an almost typical case of onyala. The latter who died bled from the vagina and nose but the only bulla found was in the larynx though petechiae were numerous in the abdominal viscera. The third patient was a half-caste boy of 12 years with epistaxis and haematuria and petechiae on trunk and limbs and subconjunctival haemorrhages but no bullae on tongue or buccal mucosa. Platelets numbered only 26,900 per cmm, leucocytes 8,200. After a blood transfusion the haemorrhage ceased and recovery was rapid. Was this another case of onyala or one of Werthof's purpura (essential thrombocytopenia)? The case occurred in an onyala district (Mashona land) and the patient had had a malarial attack a year before. The question is not a purely academic one for it raises yet another. Is onyala the same as Werthof's disease? The thrombocytopenia is a prominent feature of both, are the usually noted differences essential? See this *Bulletin* 1944 v 41 428-427 where other references are given.

H. Harold Scott

LOWEY J. F. A Case of Transient Successive Pulmonary Infiltration (Loeffler's Syndrome) associated with Trichuriasis. *Ann Intern Med* 1944 July, v 21 No 1 130-35. 10 refs.

A somewhat unusual case of trichuriasis in that none of the early gastrointestinal symptoms was present nor any oedema of the face or puffiness of the eyelids although a biopsy specimen of the deltoid showed 100 larvae per gramme. The symptoms were typical of Loeffler's syndrome of transient infiltration of the lungs, with eosinophilia 23 per cent of a total of 22,000 leucocytes per cmm. on admission. Loeffler himself thought that many of these cases were tuberculous in origin, others have remarked on the association of this syndrome with some form of allergy—asthma (Breton) to ligustrum which flowers in May and June (Engel). *Ascaris lumbricoides* (Widd) and now *Trichinella spiralis*. Since infestation by this last is estimated to have an incidence of about 20 per cent in the United States and many cases are subclinical, with less than 100 larvae per gramme of muscle the author suggests that in all cases of Loeffler's syndrome skin tests should be carried out for trichuriasis and if needed biopsy examinations.

H. Harold Scott

JONES S H & SOUDERS C R Eosinophilic Infiltration of the Lungs (Loeffler's Syndrome) *New England J of Med* 1944 Sept 7 v 231 No 10 356-8 3 figs. [12 refs.]

The case is reported of a negress 33 years old complaining of cough worse at night and fatigue. She had had similar attacks in the two preceding autumns. X rays showed localized infiltration of one lung with impairment of resonance and localized silulant râles. Tuberculosis was suspected or a neoplasm. Blood examination gave 10,350 leucocytes per cmm with 48 per cent eosinophiles. No cause could be found no tubercle bacilli no helminth ova a negative reaction for trichiniasis. Four weeks later the white cells numbered 8,400 per cmm eosinophiles 27 per cent and three weeks later still 6,500 and 9 per cent. Recovery seemed to be complete. In spite of no reaction being obtained to eighteen inhalant and food allergens endermically the authors believe that the syndrome is an allergic manifestation of at present unknown aetiology.

H. Harold Scott

RITCHIE E A A Tropical Eosinophilia: an Aetiological Inquiry *J Roy Army Med Corps* 1944 Oct v 83 No 4 177-82 2 charts & 2 figs.

COORAY G H Observations on Malignant Disease in Ceylon based on a Study of Two Thousand Two Hundred and Ninety-Five Biopsies of Malignant Tumours *Indian J Med Res* 1944 May v 32 No 1 71-91 2 graphs [25 refs.]

Although biopsy material from a pathological laboratory must fail to provide a complete view of the incidence of cancer in any particular country, the information it provides may nevertheless be of great value. Its limitations are perhaps exemplified by the fact that among the 2,295 examinations considered in Dr Cooray's paper there were only nine examples of hepatic cancer—a figure which one would think can hardly represent the frequency of this form of malignant disease among the people of Ceylon—and the figures for buccal cancer do not give a correct notion of its prevalence because as Dr Cooray points out very many of these cases are so advanced on admission to hospital that no microscopical examination is required for a correct diagnosis. Among several interesting facts it may be noted that of the biopsies on material from women 67.8 per cent represented cancer of the reproductive organs including uterus (41.7 per cent), breast (18.5 per cent) and ovary (7.6 per cent). The majority of uterine cancers arose in the cervix. There were 35 instances of chorion-epithelioma which accounted for more than half of all the cases of cancer of the uterine body. Cancer of the buccal cavity (8.5 per cent) and skin (7.7 per cent) were the next most common sites in women.

Among men cancer of the penis accounted for 27 per cent, buccal cancer for 21.8 per cent and skin cancers for 19.5 per cent of all cases. Of the skin cancers 61 per cent arose in connexion with chroma ulcers of the leg which are very common throughout the island; another frequent form was malignant melanoma arising in the sole of the foot.

[When contemplating these figures one is impressed by the large number of cancers which are allowed to occur because straightforward measures of prevention are not employed. Circumcision in childhood would entirely prevent the occurrence of penile cancer and there seems little doubt that the incidence of buccal cancer would be greatly reduced by abstention from the chewing of betel nut.]

Harold Hurrens

KENNAWAY E. L. Cancer of the Liver in the Negro in Africa and in America. *Cancer Research* 1944 Sept v 4 No. 9 571-7 2 figs. [44 refs.]

The high frequency of primary cancer of the liver in African Negroes is well known. According to BERMAN who has collected valuable data on this subject cancer of the liver formed 37.4 per cent. of all the cancers observed among the Bantu in the Union of South Africa Portuguese East Africa Kenya Tanganyika Belgian Congo and French Equatorial Africa furthermore Berman says that among the natives who come to the gold mines from Portuguese East Africa cancer of the liver is about six times more frequent than among the natives of the same race who come from other areas. Among the West African Negroes of Senegal Sierra Leone and Nigeria cancer of the liver forms 18.7 per cent. of all the recorded cancers. In contrast with these figures Kennaaway points out the Negroes of the United States though descended from the West African races are not subject to a high incidence of hepatic cancer. These facts among others suggest to Kennaaway that the high incidence of cancer of the liver in the Negro in Africa does not depend on genetic characters alone but may be due to some extrinsic environmental factor which could be identified if sought. The artificial induction of cancer of the liver in rats and mice by certain compounds and the prevention of this sequel by dietetic regulation might give an encouraging lead to such an investigation in the human subject. A brief abstract of this paper is not quite satisfactory it should be read in the original.
Harold Burrows.

GENERAL ENTOMOLOGY

KEILIN D. Respiratory Systems and Respiratory Adaptations in Larvae and Pupae of Diptera. *Parasitology* 1944 Sept v 39 Nos. 1 & 2, 1-66 54 figs. 2 pls. (1 coloured) [135 refs.]

The author here brings together the result of many years research into the morphology of the spiracles and tracheae of Dipterous larvae and pupae. He expressly omits his studies on the physiology of respiration and confines himself to structure.

The first part of the paper deals with respiratory systems in Dipterous larvae. It relates to the subjects in which the readers of the *Bulletin* are directly interested at many points for instance it strengthens the grounds for the classification of Diptera it gives a fuller knowledge of the comparative morphology of structures on which we rely in identifying larvae. It describes the structure of spiracles and of the perispiracular glands the waxy hydrophobic secretion of which is thought to help in excluding water from the tracheal system of aquatic larvae.

The second part of the paper is concerned with modifications in respiratory structure which tend to fit larvae and pupae for life in water or as parasites, or (in viviparous species) for intra uterine life. Its value to our readers is that it will relate their particular knowledge of these structures in mosquitoes Oestrids, etc. to more general studies.
P. A. Buxton

BARRETO M. P. & COUTINHO J. O. Sobre o género *Tarniorkynchus* Arnaldus, 1891 com a descrição de três novas espécies do subgénero *Tarniorkynchus* (Diptera, Callitidae). [Three New Species of *Tarniorkynchus*.] *Arquivos de Hygiene e Saúde Pública* São Paulo 1944 May v 9 No. 21 53-63 9 pls. [28 refs.] English summary

COSTA O G Furuncular Myiasis *Arch Dermal & Syph* 1944 July \ 50 No 1
36 2 figs

A man 18 years of age a rural labourer presented himself for treatment on account of small acuminated swellings like furuncles 40 to 50 in number on the back and thighs. They caused some pain especially at night they had been present for five months at first as minute swellings then becoming more tense and painful and of a violet colour with a red halo and a purulent secretion. As the lesions opened the tail of a parasite could be seen which proved to be the presenting end of a larva of *Dermatobia hominis* (cyaniventris). These swellings are known in Brazil under the names Berne Torcel or Oura. This form of myiasis is seen in Europe caused by *Hypoderma diana* or more rarely *H. bovis*. In the United States caused by the latter most commonly and rarely by *D. hominis* (cyaniventris). In South America it is associated with the list named
H Harold Scott

MANOABEIRA O Filho & CALINDO P The Genus *Flebotomus* in California *Imer J Hyg* 1944 Sept \ 40 No 2 182-98 26 figs. on 3 pls. [31 refs.]

SMITH C N & GOUCK H K Sprays for the Control of Ticks about Houses or Camps. *J Econom Entom* 1944 Feb \ 37 No 1 85-7

It is not practicable to control ticks over wide tracts of open country by the spraying of vegetation but the authors show that it is possible to bring about reductions up to 90 or 95 per cent in the numbers of ticks (*Dermacentor Ambyomma* *Ixodes*) in the immediate vicinity of camps by the use of suitable sprays. The moulting and migration of ticks soon leads to reinfestation but usually a reduction of at least 75 per cent was still noticeable after one week. The most successful mixture contained 1.92 ounces of sodium fluoride 0.61 fluid ounce of nicotine sulphate (40 per cent nicotine) and 0.125 ounce of neutral soap to one gallon of water and was applied at the rate of 75-175 gallons per acre. This causes some burning of the vegetation. It had no apparent action on chiggers (Trombiculid mites). Other sprays which gave satisfactory results contained pyrethrum with IN 930 (isobutyl undecylene sulfoxide) as activator diluted orthocyclohexylphenol or nicotine sulphate alone (1 part of 40 per cent nicotine sulphate in 200 parts of water). The last gave only a temporary reduction for two or three days but was not injurious to vegetation.

V B Hugglesworth

ROBINSON G G More Cases of Abnormal Development in the Argasid Tick *Ornithodoros moubata* Murray *Parasitology* 1944 Sept \ 38 Nos. 1 & 2 95-7 2 figs. [10 refs.]

BUSVINE J R Simple Experiments on the Behaviour of Body Lice (*Siphonou lata*) *Proc Roy Entom Soc of London Ser A General Entom* 1944 Mar 28 \ 19 Pts 1-3 22-6

The author wants to know how a man becomes infested with body lice and to study the travels of these insects under natural circumstances. His method is to release lice on or near a clean volunteer and to search for them after an interval.

If one takes a lousy shirt off a man and examines it the lice are found almost motionless generally against seams but it may well be that when the shirt is being worn and they are in the dark they run about. If one releases adult lice at one spot under a woollen vest on a clean volunteer and waits two hours one finds that on an average they have moved about a foot measured in a straight

FAUST E. C. Diseases in the Tropical War Zones. IV The Diseases of the Middle East, India, Assam and Burma. *Gastroenterology*, 1944 June v 2 No 6 395-411 9 figs. [figs. 23-31]. [19 refs.]

In this contribution Professor Faust continues his brief account of the diseases encountered in various parts of the world. The term Middle East does not in this paper include the Mediterranean area but does include S.E. Arabia, Iraq and Iran. The account is given by diseases as before see this *Bulletin* 1944 v 41 966-967] and is illustrated by distribution maps. Some explanatory matter on transmission is added and the whole forms a skeleton account of the diseases to which American troops may be exposed. *Charles Wilcocks.*

BOOK REVIEW

COOLEY R. A. [Senior Entomologist] & KOMIS Glen M. [Associate Entomologist]. The Argasidae of North America, Central America and Cuba. The American Midland Naturalist Monograph No. 1. 1944 June 152 pp. 57 figs. & 14 pls. Edited by Theodor Just, Published by the University Notre Dame Notre Dame Ind.

Since about 1896 there has been a great increase in knowledge of the species of *Ornithodoros* of North America, and it has been realized that relapsing fever in man is rather widespread, though uncommon and that several species of this genus can transmit the infection. The new work has come out in a considerable number of brief papers and it is welcome to see much of it brought together and unified. The author a ripe scholar has been a leader in these new developments.

In North America twenty five species of *Ornithodoros* occur and it is known that five of them *kerrisi ferrugalis parkeri talaje* and *rudis* occasionally transmit spirochaetes to man and cause relapsing fever in every case it seems that the infection in man is an overflow from some other mammal.

The book is a contribution to systematics but many interesting biological points emerge from it. One is the extraordinary range of hosts of some of these ticks. *O. stegani* feeds on bats also man *parkeri* on rodents burrowing owls and man. The point is well seen in the lists of recorded hosts of each species at the end of the book (though it is not clear that the tick has actually been recorded feeding in all cases.)

The book is concerned mainly with identification, and descriptions of species with emphasis on points of distinction of larvae. It provides synonymy keys to genera maps of distribution and excellent photographs and line drawings of the ticks themselves. In the author's view *Argas*, *Otiobius* and *Amblyomma* are valid genera, in addition to *Ornithodoros*. *P. A. Buxton.*

TROPICAL DISEASES BULLETIN

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[No 3

SUMMARY OF RECENT ABSTRACTS *

III MALARIA

Epidemiology and Distribution

HACKETT (p 998) writes of the value of spleen surveys in malaria they revealed areas of endemic malaria in Italy and Albania and are of the greatest value in estimating the results of control measures and in comparing malaria intensity in different places But spleen surveys should not rule out blood examination and where the two are performed they should be done on the same persons He advocates a method of spleen assessment in which numbers from 1 to 5 are given according to size The size of the average enlarged spleen is significant it tends to be higher the longer the transmission season

MAZZEO and SEMENTINI (p 352) report on malaria in part of the Province of Naples PETAZZI (p 353) on malaria at Durazzo COLUZZI (p 353) on malaria at Valona and in Epirus These papers are of local interest

PARADE (p 820) reports two cases in which infection was apparently contracted at Innsbruck Austria.

LINDBERG (p 637) gives an account of malaria in Iran about which little has previously been published. In the Caspian provinces *Anopheles* are not found over 2 000 metres but in the mountain valleys malaria is common in the summer months *A. superpictus* is the probable vector there but *A. maculipennis* and *A. elutus* are suspected elsewhere Several other species are reported from different areas All the three common forms of malaria are seen but distribution over the country is patchy ZADEH (p 638) also gives information on malaria and *Anopheles* of Iran

ZUMPT and MINNING (p 4) report on malaria in Southern Russia during the German occupation there is nothing unusual in the information given PLATONOV (p 636) notes that *P. falciparum* infection is endemic in south west Siberia in the flood plain of the river Ohl

WILSON and NOTLEY (p 90) report on malaria in Southern Somalia (formerly Italian Somaliland) The vector is *A. gambiae* which breeds in irrigation water flood water rain water or pools in permanent rivers The transmission season is usually short and the disease mostly epidemic. In places with a very short season the spleen rates tended to be higher in adults than in children with a

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1944 v 41 References to the abstracts are given under the names of the authors quoted and the page on which the abstracts are printed.

rather longer season the rates were equal but the size of the spleen increased with age with a still longer season the rates were equal or decreased with age and the size of the spleen was similar at all ages.

LAOUILHEAU (p. 999) found a spleen rate of 40 per cent in Libreville, Gabon at the beginning of the dry season. Infections with *P. falciparum* were rather more numerous than those with *P. vivax*.

SARMENTO (p. 987) discusses the epidemiology of malaria in Camacupa (Angola) a hyperendemic area in which *P. falciparum* is the commonest parasite.

SIVALINGHAM (p. 718) gives the results of a survey of spleen and parasite rates in Ceylon after a severe epidemic of malaria had affected the wet and intermediate zones of the island. *P. malariae* was the commonest parasite of all zones.

YAO (p. 88) refers to the incidence of malaria in China in the low-lying region it is mild and *P. vivax* predominates but in the south-western provinces, especially along the borders of Indo-China, Thailand and Burma, the common infection is with *P. falciparum*. In 1939 thousands of workmen died of subtropical malaria on the Yunnan Burma highway. A list of *Anopheles* of Free China is given—*A. minimus* is the chief vector in the south-west but *A. jeyporiensis candidiensis* is also important. Yao *et al.* (p. 999) report on a malaria survey of the south-west terminus of the Yunnan Burma highway where *A. minimus* is the chief vector (though *A. hyrcanus sinensis* and *A. jeyporiensis candidiensis* have been found infected). *P. falciparum* is the commonest parasite. The heavy malaria season is the last quarter of the year. YU and LING (p. 89) also write of the severe endemic malaria of Yunnan. In a description of a series of patients they emphasize the protean manifestations of the disease. In obscure cases sternal puncture and the ephedrine provocative test have been found useful. WINTERBOTTOM and ARDEN (p. 255) report malaria in Brisbane, Australia, which is much farther south than the limits of any recorded outbreak since 1900. It seems likely that the patients were infected by *Anopheles* which had themselves picked up infection from soldiers returned from malarious war areas. *Anopheles annulipes*, a proved vector, exists as far south as Tasmania.

FAUST (pp. 91-938) shows that the steady decline in malaria mortality and morbidity in the United States has continued through the years 1941 and 1942. Figures are given for the various States.

DOWNS *et al.* (p. 445) have provided a comprehensive report on malaria in Trinidad and Tobago where the population has been greatly increased on account of war time activity. Malaria causes as many deaths as pulmonary tuberculosis and many more than enteric fever according to published figures. About 83 per cent. of diagnosed infections were due to *P. falciparum* in the period concerned. The spleen rate in children varies from 3.4 to 53.1 per cent. and the parasite rate varies directly with the spleen rate. Of the 13 *Anopheles* found, two are vectors—*A. aquasalis* which breeds in coastal brackish water and *A. bellator* which breeds in bromeliads parasitic on the shade trees of coconut plantations. It is noted that about half the area of Trinidad is free from malaria.

SCHIAVI, DE MELO and CÔDA (p. 915) report cases of quartan malaria from the State of São Paulo, Brazil.

ALBERTO ALVARADO (p. 633) gives an account of malaria in Argentina in which he shows that even *P. falciparum* infections are relatively mild.

Aetiology

SHUTE (p. 255) has succeeded in producing human infection with sporozoites of *P. falciparum*, *P. vivax* and *P. ovale* which had not been in contact with the salivary glands of the mosquito but were present in ripe oöcytes. There had previously been controversy as to whether or not this was possible.

ANGELINI (p 181) has found malaria parasites in normoblasts the invasion of immature erythrocytes is rare and is seen only in heavy infections

MATILLA and APARICIO (p 530) claim to have found extracellular malaria parasites constantly in the bone marrow of patients undergoing malaria therapy

SCHWETZ (p 529) discusses the morphological variations seen in *P. falciparum* which in the past have led to suggestions that different species exist. He however relates these differences to the various degrees of immunity in the patients or to changes produced in the preparation of blood slides. The presence of numerous very young rings in non immune persons indicates that the febrile attack is due to malaria but the presence of older forms in immune individuals means that the attack may be due to some other febrile illness in a malaria carrier

KITCHEN and PUTNAM (p 5) have studied the morphology of gametocytes of *P. falciparum* of certain strains and have found that there is so much variation within the strains that attempts to identify strains by these characters would be extremely difficult. The outstanding characters of gametocytes in general however can be defined they are usually sausage-shaped rather than crescentic in males chromatin and pigment occupy both central and outlying zones but in females they tend to be central male pigment is diffuse and light but female pigment tends to be compact and dark in males individual chromatin is diffuse and vesicular but in females it is compact and vesicular

DE ZULUETA (p 259) states that he has observed schizogony of *P. falciparum* in the peripheral circulation in 2-4 per cent of a series of cases in Bogotá he thinks that certain strains exist which normally reproduce in this way and that in these cases such forms are of less grave significance than usual

KIKUTH (p 724) concludes from an examination of the evidence that the tendency to relapse after 8 or 9 months is a feature of infection with certain strains of *P. vivax* particularly those of European origin and that it is not dependent on factors outside the parasite itself. It is now generally held that the exoerythrocytic stages are those which persist in these cases. Treatment to prevent these relapses is not very satisfactory though plasmoquine (pamaquin) has some effect especially when combined with atebryn (mepacrine) as in Atepe-tahlets (atebryn 0.1 gm. plasmoquine 0.005 gm.)

Mosquito Transmission

ROSS and ROBERTS (p 256) have produced an atlas of 18 Old World *Anopheles* important in malaria.

KALANDADZE and SAGATELOVA (p 916) make the point that anopheline eggs (or larvae) may survive at the bottom of depressions once collections of water which have been dried in the course of anti larval operations [it is difficult to see how larvae can persist unless the drying is very incomplete] When the depression fills (by rain or irrigation) the water becomes repopulated with larvae from these eggs. They have therefore made experiments on the resistance of eggs of *A. maculipennis* to desiccation and have shown that it depends to some extent on the stage of development attained by the embryo but more on the retained humidity of the soil. Control by the drying of water collections therefore can be successful only if desiccation is complete since in the presence of slight moisture the eggs can survive more than a week. Anopheline eggs are more resistant than culicine. [This is obviously an important subject in relation to the periodical drying of rice fields or irrigation channels elsewhere.]

SHIPITSINA (p 719) has studied the area of water surface which is filtered by the larva of *Anopheles* in feeding and relates this in the various larval stages to the use of Paris green. Details should be sought in the original abstract.

SHUTE (p. 528) sums up the position in England with regard to the possibility of malaria transmission by the indigenous species *A. axfieldi*. The only efficient vector is *A. maculipennis* *axfieldi*, which is the British water breeder and the transmission period is short, Jun to September. He discusses preventive measures which could be taken if malaria were once more established.

WILLIAMSON (p. 830) has investigated, in England, the relation of ferruginous water to the breeding of *A. maculipennis* *axfieldi*. These waters are not themselves harmful to the larvae except that they are deficient in larval food. They lack algae whose growth is probably inhibited by the presence of colloidal iron and associated peaty substances in the water.

OLZCHA (p. 256) found that almost all the female anopheline eggs collected in the Polish province of Posen were *A. maculipennis* *mesasiatica*. The mosquitoes bred out were kept in a warm room and fed on pigs' blood diluted with half the volume of water-sugar being added. They sucked this up from cotton wool moistened by the diluted blood. JIKOV and KRASIKOVA (p. 917) have shown that *A. maculipennis* *mesasiatica* hibernating in cellars in Siberia, haunts the living quarters throughout the winter and that they breed during that period. It was demonstrated that they lay eggs in the moist soil of flower pots in the houses. Mosquitoes can become infected during the winter and the parasites can complete their development in the cold season. House infections are therefore of epidemiological importance. It was known that some species of *Aedes* may lay eggs in mud or places where water is likely to collect. The observation that anophelines may do the same is most interesting.

DAVIES (p. 448) reports observations on the breeding of *A. claviger* (*trifurcatus*). Details cannot be further abstracted.

DE MEILLON (p. 182) has written an account of the entomology of malaria in Africa south of the Sahara, but this cannot be summarized here.

In the *British Medical Journal* (p. 256) there appeared an editorial note in which it was stated that *A. gambiae* *melas* (subsequently known as *A. melas*) the important vector in Freetown, breeds in one form only of mangrove swamp and that this form grows in limited clumps, and can be eliminated.

LAUCHEL and CAMROUZY (p. 94) report infection in *A. gambiae* *A. fuscipes* and *A. splendidus* in the French Cameroons. (The last mosquito is referred to as *Neocellia splendida*. *A. splendidus* is a Far Eastern species; it is therefore uncertain what species is meant perhaps *A. maculipennis*.)

SCHWETZ (p. 90) has investigated the incidence of malaria in relation to altitude in the Belgian Congo and concludes that the upper limit may be taken as 1,750 metres. *A. gambiae* is not found above this height. The absence of

at high altitudes seems to be due to the absence of a vector rather than to the absence of cold in impeding the development of the malaria parasite in

IVY (p. 6) show that *A. gambiae* is the only important
land. VAX SORREY (p. 257) also found *A. gambiae* in
Somaliland, though he states that it has not previously
species are mentioned.

(p. 640) have investigated the Anophelids of
000 feet and breeds chiefly in pools in the
area, including domestic collections. This
and is probably responsible for the
feet. *A. fuscipes* is rarely found.

the longevity of *A. calicifacies* under
humidity. Details should be sought

to expectation. *A. calicifacies*
found there. *A. farwsi* is also

negligible as a carrier and shows little inclination to enter human dwellings differing in this respect from *A. varuna* of the Jeypore Hills where it is an important carrier. The chief vector is *A. stephensi mysorensis*.

WHITE (p 721) shows that the chief vector in the Hazaribagh Ranges is *A. fluviatilis* and that *A. culicifacies* transmits to some extent from July to September. An outbreak due to increased breeding of *A. stephensi* in the wells of one town is reported.

VISWANATHAN and LIAO (p 641) note that *A. fluviatilis* tends to enter dwellings soon after dusk and that it tends to feed early though feeding goes on throughout the night.

KNOWLES and BASU (p 531) have found experimentally that temperature appears to be a more important factor than humidity in the transmission of malaria by *A. stephensi*. The heaviest gland infection with *P. vivax* took place at 80°F and the most rapid development at 90°F for both *P. vivax* and *P. falciparum* (9 days). Similar results were found with *A. annularis*.

ROY (p 449) has shown that *A. subpictus* can be infected under laboratory conditions but that the sporozoite rate is much less than that of *A. stephensi*. He concludes that although natural infection may occur in the more humid parts of India the danger from *A. subpictus* is negligible.

WHITE *et al* (p 720) show that in the Orissa coastal plain *A. annularis* is the chief vector of malaria though 17 other species have been found and *A. aconitus* has also been demonstrated with sporozoite infection. *A. annularis* breeds in still water containing vegetation and filamentous algal growth chiefly in tanks and ricefields. Its transmission season is from September to November or December. Malaria epidemics are superimposed on considerable endemicity; they are very local and apparently depend on biological factors favouring *A. annularis*.

DAS (p 89) notes infection found in *A. aconitus* in East Bengal. Hitherto this mosquito has not been considered an important vector in this area.

ROBERTS (p 641) brings evidence which indicates that *A. annulipes* is as efficient a vector of *P. vivax* and *P. falciparum* as the more well-known carrier *A. punctulatus moluccensis* of Australia. It would be unwise to concentrate gametocyte carriers in any area where *A. annulipes* is abundant.

RENN (p 182) discusses the surface forces which operate to induce the grouping of *Anopheles* larvae around the stems of aquatic grasses.

EYLES and COX (p 642) have estimated *A. quadrimaculatus* populations by a technique of marking similar to that which has been used in work with *Glossina*. EYLES (p 642) describes the method in detail. JONES (p 532) has noticed that *A. quadrimaculatus* in the Mississippi valley may remain so long in a favourable shelter that their abundance may not indicate very recent production from a breeding place. He has proved that a female can survive for at least 35 days in nature. He comments on the effect of water fluctuations in a reservoir on mosquito breeding. HIXSON (p 532) discusses the larval population of *A. quadrimaculatus* in relation to the fauna of a lake and a pond in Florida. *Gambusia affinis* was the predominating fish and its effectiveness as a predator increased with the size of the mosquito larvae.

SISK (p 355) notes the importance of controlling the breeding of *A. quadrimaculatus* in N. Carolina in view of the fact that many of the men who will return after the war from military service will bring the infection back with them.

BOYD and RUSSELL (p 92) have failed to find any simple genetical explanation of the fact that infection of *A. quadrimaculatus* with *P. vivax* is irregular.

KUMI and KUNIGA (p 643) have shown that in Costa Rica and El Salvador the most malarious months of the year were usually preceded by an increased prevalence of *A. albimanus*. WEATHERSBY (p 643) shows that *A. albimanus*

though a noted transmitter of malaria, prefers horse to man, in the proportion of about 20 to 1. PRITCHARD and PRATT (p. 722) has compared a light trap and an animal trap (baited with horse or calf) for use in connexion with *A. albimanus* in Porto Rico. Each has advantages and the best results are obtained by the use of both.

BRUCE *et al.* (p. 93) give a list of the *Anopheles* found in British Guiana. In the BRITISH GUIANA MEDICAL ANNUAL, 1943 (p. 529) is a report on malaria. *A. darlingi* is the chief vector and is the most prevalent anopheline. Infection was not found in other species dissected, but it is thought that *A. larai maculatus* (probably *A. aquasalis* and *A. oswaldoi*) may be a vector in George town and elsewhere. *A. albimanus* an important vector in Brazil, rarely enters houses in British Guiana. No anophelines breed in the bromeliads of British Guiana.

CAUSEY *et al.* (p. 644) have published an illustrated key to the eggs of 30 species of Brazilian *Anopheles*.

CORREIA (p. 1006) describes the vectors of State of São Paulo. *A. darlingi* and *A. larai maculatus* are the chief transmitters but *A. cruzi* is a vector in forest areas breeding especially in trees parasitized by bromeliads [*cf. A. bellator*]. More work is necessary to determine the part played by *A. strodei*, *A. albimanus* and *A. noroestensis*.

DA FONSECA and DA FONSECA (p. 93) have investigated the transmission of malaria in an island off S. Paulo (Brazil) and have found *A. oswaldoi oswaldoi* and *A. oswaldoi guarayensis* to be capable of infection with *P. vivax* and *P. falciparum*. The latter mosquito was probably responsible for epidemics of malaria in 1940 and 1941.

FRAGA (p. 447) notes that *A. cruzi* and *A. bellator* are the probable vectors of malaria in Paranaguá, Brazil. They breed in the bromeliads which are parasitic on local vegetation.

Transfusion Malaria.

DAS GUPTA (p. 92) records a case in which transmission of *P. falciparum* occurred through transfusion of blood from a donor who though he had no history of previous malaria, had just returned from a malarious district, and was in the incubation period of the disease, when he was bled. If it is impossible to eliminate the risk of infection the recipient should be given 5 grams of quinine thrice daily for three days after transfusion.

BARTOSHEVICH (p. 8) reports malaria transmitted by transfused blood (in one case preserved for 3 days) from a donor who though negative to blood examination, came from a malarious district. It is thought that repeated removal of blood from this donor activated a latent *P. vivax* infection.

As a result of careful tests LOJNER and NEWHouser (p. 91) conclude that the risk of transmission of malaria by transfusion of plasma is practically non-existent.

Pathology and Immunity

DHAYAGUDE and PURANDARE (p. 533) have made pathological studies in cerebral malaria for details of which the original abstract should be consulted. It may be noted that they state that *P. vivax* as well as *P. falciparum* can produce severe cerebral damage and that in 7 of the 33 cases in which the species of parasite was determined, *P. vivax* was the only one found, and was therefore presumably responsible for the cerebral lesions.

LENDRUM (p. 822) suggests that tissues suspected of being malarial should, for pathological examination be fixed in formalin-free fluid, and gives details of a method in which potassium bichromate and mercuric chloride are used.

CLARK (p 1001) states that immunity in malaria is never absolute and may be broken by fatigue, exposure underfeeding or the introduction of fresh strains of parasites. In villages in the Panama Canal zone there is a significant incidence of malaria at all ages. In a Negro labour force in Cuba who had had lifelong exposure to malaria in Haiti there was sufficient reaction to malaria to decrease the efficiency of the labour force.

SCHILLING (p 723) brings evidence which indicates that protective antibodies appear in the blood some hours (and are most readily demonstrated 12-18 hours) after the height of the fever.

COGGESEALL (p 94) has given an outline of the process of immunity in malaria the paper should be consulted in the original.

Diagnosis Tests

WOLMAN (p 181) gives a stain formula which he has found to give more satisfactory results than Field's stain of which it is a modification. SINGH and BHATTACHARJI (p 822) describe a rapid water-soluble stain for malaria parasites. Details are given in the original abstract. HEIMBERGER (p 823) also describes a new method of preparing slides for staining. KERN and KUSTNER (p 644) describe a new staining technique. CRAWFORD (p 1002) describes the staining of blood films and in comment on this paper SEUTE makes certain criticisms and suggestions. These should be sought in the original.

DIXON (p 723) refers to the use of Leishman's stain in demonstrating malaria parasites in cerebral tissues and in comment CORSON recalls the method of obtaining tissue by puncturing the brain of the cadaver through the orbital plate of the frontal bone.

DENHOFF and PFER (p 918) refer to the difficulties in the diagnosis of malaria in troops under field conditions in the south west Pacific especially in men who have been taking suppressive drugs. In such cases however they advocate repeated blood examinations at intervals of 4-8 hours and state that if malaria is present parasites are usually found in thick smears before the sixth examination but that the parasites may be atypical in appearance. They give directions for staining which should be sought in the original abstract. In comment SEUTE makes a number of criticisms of the authors' methods.

In writing of some common misconceptions of malaria LOWE (p 997) states that it is wrong to think that untreated malarial patients in whose blood parasites cannot be found are common. A properly stained thick blood film still remains the most reliable method of detecting infection and a negative result usually rules out the disease. Sternal puncture rarely shows parasites when a thick blood film fails. He points out however that the presence of parasites is not necessarily an explanation of the symptoms.

AITKEN (p 95) however finds sternal puncture a useful diagnostic procedure in cases in which examination of thick blood films is negative. Malaria parasites are more numerous in the sternal marrow than in the blood but the author draws attention to some of the difficulties in interpreting the results of sternal puncture.

YU and YING (p 95) find that sternal puncture often gives positive results when blood examination is negative both in *P. falciparum* and *P. vivax* infections. The ephedrine provocative test is also useful but not to the same extent as sternal puncture. RUMBALL *et al* (p 95) also report on the value of sternal puncture where blood examination is negative especially in latent malaria. In the diagnosis of pernicious malaria HERMITTE (p 189) advocates sternal or even liver puncture if the blood is negative. If all are negative subtertian malaria can be excluded [but as CORSON points out in comment microscopic diagnosis depends on good technique and where this is not possible clinical experience should not be overlooked].

PACKCHANYAN (p. 823) notes that exposed blood films may become contaminated with the excretion of flies containing flagellates.

DAWKE (p. 364) brings evidence to show that malaria may be the cause of false positive syphilitic serum reactions. In general these reactions become negative within 10 days of the institution of anti malarial treatment, but occasionally this period is longer. HACKER (p. 8) found more positive serum tests (Wassermann, Meinecke and Kahn) in patients suffering from first attacks of malaria than in relapses.

SAGEL (p. 356) claims that in naturally induced malaria there occurs a monocytosis which is not found in inoculation malaria and that the difference is due to the stimulation of the reticulo-endothelial system by the sporozoites. He thinks that it may justifiably be assumed that an exoerythrocytic phase of development occurs in man.

Clinical Findings

BOMFORD (p. 730) has attempted an analysis of the frequency of attacks of malaria in the staff of a hospital in West Africa—the numbers of persons on which observations were made are admitted to be small, but the results of the enquiry suggest certain possibilities. The attack rate varied according to rank—low in officers and nursing sisters moderate in sergeants high in private soldiers. This suggests an influence connected with housing food and opportunities for rest and recreation. Incidence was high in those doing night duty it was not related to the use of alcohol or to obvious carelessness but seemed to be connected with other causes of ill health e.g. diarrhoea. Inadequate convalescence is a potent cause of early relapse. Individuals apparently vary in their liability to attacks of malaria.

OGBOYE *et al.* (p. 1000) regard as unjustifiable the tendency to regard all fevers in East African natives as malaria until the contrary is proved. Of 512 Africans admitted to hospital for fever 384 proved to be cases of uncomplicated malaria but in 116 cases other diseases were responsible for the condition, the finding of malaria parasites being incidental. Among the diseases responsible were relapsing fever typhoid amoebiasis pneumonia acute respiratory disease and bacillary dysentery. In assessing the significance of positive slides of the blood of Africans attention should be paid to the state of immunity the clinical condition and the intensity of the infection. Men were considered immune if they had spent their boyhood in regions where malaria is prevalent for more than half the year. In such patients quite commonly there were malaria parasites in the blood but the patient was not suffering from clinical malaria.

CARNEY and LEVIN (p. 730) note that 9.7 per cent. of a group of Italian prisoners of war were found to harbour parasites (chiefly *P. vivax*) although most of these men gave no history of malaria.

STIERK (p. 536) has noted signs of pulmonary involvement in about 10 per cent. of malaria cases and a similar proportion in sandfly fever. The signs may be of bronchitis or incipient pneumonia. Sulphapyridine and quinine have been given concurrently without ill effect. SHONE and PASSMORE (p. 184) have found auto-haemagglutination in certain cases of pneumonia associated with malaria, and in other conditions. As MORGAN points out in comment the findings bring fresh evidence of the fact that malaria predisposes to respiratory infections.

RAVEN (p. 537) writes of the relation of malaria to surgery—the disease may be provoked by injuries burns or operations or may simulate conditions calling for surgical interference.

BAUGÉ (p. 639) found 73 mixed infections with various malaria parasites in 15,606 blood examinations in Tunisia and 30 in 8,531 examinations in the

south of that country. More than one-third of the mixed infections were in children under 10. They were more severe than ordinary infections.

ECKSTEIN (p. 361) discusses the peculiarities of malaria in childhood as he has seen it in Turkey. In particular he mentions the association of malaria with malnutrition and of malaria with noma which is relatively common.

THORNHARD NEUMANN (p. 362) records his observations in cases of chronic malaria with splenomegaly. Treatment with quinine, ephedrine, arsenic and iron was successful but he points out the frequent association with other diseases such as hookworm infection, syphilis and amoebiasis which need treatment.

BAUM (p. 450) reports two cases of chronic malaria in which the symptoms were those of persistent anaemia without demonstrable parasites in the blood except on one occasion in one patient. Treatment with iron was ineffective but antimalarial drugs produced rapid cure. SEELIG and HEMMING (p. 724) report from India a number of cases of megalocytic anaemia as a sequel of malaria. These were probably nutritional in origin and required anti-malarial treatment supplemented by iron, liver and a full diet.

REISGER ARESHEVA (p. 919) has studied the question of hypovitaminosis C in relation to malaria and pregnancy. The condition is provoked by malaria and in spring the vitamin C content of the placenta of malarious women is lower than that of healthy women on the same kind of diet. It is thought that certain symptoms—petechiae, stomatitis, abortion—cannot be explained fully on the basis of malaria alone but that deficiency of vitamin C plays some part.

VOINO-YASENETSKI (p. 645) in a series of post mortem examinations has found no support for the view that colitis can be caused by malaria.

EDGE (p. 727) has examined the statistical evidence bearing on the subject of the relation between malaria and nephritis in the British West Indies but from the official data has failed to find information which throws light on the subject.

BERLIN (p. 824) discusses malarial psychoses and concludes that they may result from infection with any one of the three principal species of parasite.

OGANESOV *et al* (p. 535) propose a clinical classification of malaria under the following heads: Pre-morbid form, Primary malaria, Protracted malaria, Meta-malarial disorders. These with various subdivisions they relate to the symptomatology.

PERVES (p. 354) has found *P. falciparum* in the spleen or bone marrow of three stillborn infants in a highly malarious area of the Cameroons. He has found this parasite also in the blood of the umbilical cord or in the finger blood of a considerable proportion of infants examined soon after birth. As a rule however parasitaemia and splenic enlargement of infants become apparent only after the age of 4 months with peak infection at 18 months.

The importance of early diagnosis and adequate treatment of *P. falciparum* malaria have often been stressed. MOSER and MELENEY (p. 536) once more emphasize the subject and draw attention to the difficulties. Malaria should be suspected in every patient recently returned from the tropics whatever his symptoms. Fever may be absent even in overwhelming infections. A single negative blood film is not enough to exclude malaria. In treatment mepracrine is advocated but for cerebral malaria quinine should be given by injection.

HUGHES and BOWFORD (p. 357) describe the clinical features of *P. falciparum* malaria in British troops in West Africa. Details should be sought in the original abstract but in general and under the existing conditions the disease was milder than was expected. Less than 10 per cent. of the patients could be described as severely ill. In an editorial comment in the *British Medical Journal*

[March 1945]

it is suggested that suppressive medication or other preventive measures may have been responsible for this and that the troops are now much more malaria conscious than they were in the war of 1914-18.

SIMPSON *et al* (p 359) report on a series of 4 647 cases in the South Pacific, where hyperendemic conditions exist the patients were members of the United States forces. Parasites were found in 1 184 and details are given of these men. Twelve per cent. proved refractory to one or more courses of treatment and almost half of these had *P. falciparum* infections. There was only one case of blackwater fever and only one death. It is remarked that nearly half the patients had received regular suppressive treatment at first 10 grains of quinine daily later 0.2 gm. atebm twice each week [another proof that suppressive treatment of this order is insufficient in hyperendemic areas] No significant toxic reactions were observed as a result of the use of atebm. In treatment quinine and atebm were given concurrently. SIMPSON and SAGEBIEL (p 360) describe 12 cases of cerebral malaria which occurred in the series referred to above. Details are given which should be sought in the original abstract all the patients recovered.

HUSSAIN and BROADBENT (p 359) draw attention to the fact that *P. falciparum* infection can simulate acute abdominal conditions (even acute intestinal obstruction) and that pain, with diarrhoea and blood in the stools may also apparently be due to the same infection. He records cases which cleared up on anti-malarial treatment alone.

BREWIS (p 7) reports a case of pernicious subtertian malaria in which the symptoms resembled those of blackwater fever though this was the first attack of malaria the patient had suffered, and he had taken no quinine.

WHITEHALL (p 450) describes a case of cerebral malaria with haematuria which was regarded as due to true malarial nephritis. Treatment with injected quinine and later with mepacrine was successful.

NELSON JONES (p 537) writes as have so many others during the present war of the extremely varied symptoms to which infection with *P. falciparum* may give rise and remarks that differential diagnosis involves almost the whole of medicine.

RODGER (p 728) reports a very low relapse rate in the malaria treated on a mine in N. Rhodesia, where most of the infections were due to *P. falciparum*. Immediate treatment (largely with quinine) is regarded by the author as one of the essentials in preventing relapse.

SCOTT (p 920) describes a few cases of herpes simplex of the cornea in patients with subtertian malaria in West Africa.

GEY (p 6) reports three fatal cases of cerebral malaria on board a cruiser but remarks that the element of heat stroke could not be altogether ignored the two conditions are probably closely connected. SWEDDON (p. 259) reports a fatal case of cerebral malaria and commenting upon it CAMERON (p 260) points out that in the treatment of such cases quinine should not be spared. Two even three intramuscular injections of 15 grains may be needed daily as should be given until vomiting ceases and coma is ended. FENTON RUSSELL (p 921) however draws attention to the milder types of cerebral malaria which are more common than the severe states. He does not advocate intramuscular injection of quinine because of abscess formation preferring intravenous therapy.

HAMBURGER (p 723) comments on six cases of cerebral malaria and draws attention to points of clinical importance. DON and MEYER (p 358) report an unusual case of cerebral malaria in West Africa.

Symptomless parasite carriers have been investigated by SHEINKER, SARIKIAN, REMENNIKOVA and SHISHLIAEVA MATOVA (p 817) in Russia. Most of the cases found were carriers of *P. vivax* and most had symptoms at

some time. In the majority the spleen was not palpable and a spleen survey would therefore not have been useful in detecting them. Mosquitoes are readily infected in spite of the small numbers of parasites. Treatment is useful in eliminating the carrier state. After a large epidemic the following spring there are found large numbers of carriers many of whom give no history of malaria.

GAMMIE (p 1002) reports a case of congenital *P. vivax* malaria in a child born in England.

TAREJEV *et al* (p 257) again refer to the fulminating type of malaria ascribed to *P. vivax* which they have previously described in Russia. Cerebral manifestations are common even in the first paroxysm. The prognosis is grave but immediate injection of quinine or mepacrine is a life-saving measure. POLUMORDVINOV (p 823) refers to the fulminating type of *P. vivax* infection which has caused deaths in children. Those who died showed no constitutional anomalies the main subjective symptom being severe headache. TROITSKY (p 823) reports 61 fatal cases in 1941 when there was a severe epidemic outbreak. [The history of these cases and outbreaks of pernicious *P. vivax* malaria is so unusual that it leaves the impression that the cause is by no means fully elucidated.]

PUHLMANN (p 919) points out that persons exposed to infection may complain of various mild complaints particularly in autumn or winter which are due to *P. vivax* (occasionally to *P. falciparum*). Diagnosis may be difficult and parasites may only be seen after examination of several thick films.

A study of malaria in the Caucasus has led KEKCHER (pp 258-449) to the conclusion that *P. vivax* infection does not as a rule last more than 12-18 months though in a small proportion of cases it may persist for 3-4 years and that *P. falciparum* infection usually lasts for 2-12 months. He notes a tendency to diagnose chronic malaria on insufficient evidence in those with a history of that disease.

WILCKENS (p 183) writes of certain German soldiers who were presumably infected near Lake Ladoga in N. Russia, and who exhibited long latent periods before the onset of fever.

SHUTE (p 1002) reports relapse of quartan malaria in a patient who had not lived in a malarious country for 21 years.

CRUCA *et al* (p 645) contribute a study of induced *P. malariae* infection. This cannot satisfactorily be condensed more than in the original abstract which should be consulted.

Charles Wilcocks

RABIES.

A REVIEW OF RECENT ARTICLES. XLII *

1. Virus

The question whether the virus of rabies can be transmitted from the mother to the foetus *in utero* has been studied by numerous investigators. The evidence of the earlier work was conflicting. KONRADI (*Zbl. Bakt.* I Abt. Orig. 1905 v 38 60 1908 v 47 203 1914 v 73 287 and *Ann. Inst. Pasteur* 1916 v 30 33) attributed the variable and conflicting results to the use of the rabbit instead of the more susceptible guinea-pig as the test animal for the detection of virus in the foetuses the inoculations being made subcutaneously instead of intracerebrally and the failure to keep the test animals under observation for a sufficiently long period. He succeeded in demonstrating that rabies could be

* For the forty-first of this series see this *Bulletin* v 41 p 904

transmitted from the mother to the foetus in rabbits, dogs and guinea-pigs. REMLINGER (*Ann Inst Pasteur* 1919 v 33 375) in a limited number of observations also recorded some positive results. Certain viruses and other infective agents have been propagated by their inoculation into mammalian foetuses developing *in utero* and into chick and duck embryos. OLIVEIRA and BETTENCOURT¹ have now made experiments with the virus of rabies to determine whether it can be cultivated in the embryo of laboratory animals *in utero* and whether it can pass through the placenta and infect the mother. They employed rabbits. Two strains of virus were used. A "fixed" rabbit strain which was the one then generally used for making vaccine and a "street" strain which, after recovery from an infected dog, had undergone one passage in guinea-pigs. Their general technique was as follows.—rabbits in the second week of gestation were selected and laparotomy was performed under ether anaesthesia. The syringe used for the inoculations had a capacity of 1 cc and was graduated in 1/100 cc and fitted with a fine needle 1 cm long. Quanta of virus in Milam's fluid were inoculated intracerebrally (0.05 cc) or intramuscularly into the hip (0.5 cc) of the foetuses *in situ* through the wall of the uterus which was subsequently clamped at the point of entry of the needle. In certain experiments virus was inoculated in a quantum of 0.5 cc. into the amniotic sac after the withdrawal of a corresponding amount of the fluid. In others again, quanta of 1 cc of virus were inoculated slowly into the wall of the uterus at an oblique angle. Proof of infection of the foetuses was secured by inoculation of suspensions of their brains intracerebrally into guinea-pigs and when street virus was used histological confirmation was obtained from smears of the *Cornu Ammonis* stained for Negri bodies by Lentz's method. The brains of the mothers of virus-infected foetuses were examined for the presence of possibly latent virus by histological study of the *Ammon's horn* for Negri bodies and by inoculation of suspensions intracerebrally into mice. Three of these mice were killed on the 5th, 6th and 7th days respectively, so that their brains could be examined for Negri bodies and the other mice which incidentally did not develop symptoms in any experiment were killed and their brains studied histologically for Negri bodies four weeks after inoculation.

Observations are recorded on 19 rabbits, three inoculated with fixed virus and sixteen inoculated with street virus. The results showed that the virus inoculated intracerebrally or intramuscularly into the foetuses or into the amniotic fluid, could in most cases subsequently be recovered from their brains when they were born, either alive or dead from one to eight days later. Negri bodies were demonstrated both in the brains of the inoculated foetuses and in the brains of the test guinea-pigs inoculated when street virus was used. If certain of the foetuses in the womb were left uninoculated they did not become infected with the virus. None of the 14 mothers, the foetuses of which had been inoculated with street virus, developed rabies during the period of more than six months within which they were kept under observation. Four died of an intercurrent infection. The brains of the four which died and some of the survivors were examined histologically for Negri bodies and suspensions were inoculated intracerebrally into mice, but with negative results. This confirmed that none of the mothers became infected with virus from the foetuses.

Two pregnant rabbits inoculated with street virus into the walls of their uteri, died of rabies on the 31st and 56th days respectively. Negri bodies were demonstrated in their brains histologically and virus by inoculation of guinea-pigs intracerebrally. The young of the first mother did not become infected with rabies but three of the six young rabbits of the second mother died of rabies.

¹ DE OLIVEIRA, J. C. & DE BETTENCOURT, A. *Parasitismo da placenta ao virus rabico inoculado a dois foetos de lapao. Arquivos Inst. Biol. Camera Portuguesa* 1945, v 9, No. 1 1-17 [18 refs.]

The authors state that their observations point to the placenta as the obstacle to the passage of virus from the foetus to the mother. They hope to be able to determine whether this inhibition is a phenomenon of filtration or due to some special substance which neutralizes the virus. They observe that the absence of nervous connexions between the foetus and the mother must render difficult the passage of a virus which usually travels by nervous paths.

ii *Methods of Treatment and Control*

Army doctors are immediately responsible for maintaining the health of their troops and preventing any spread of infection among them. To this end even in peace time they have to take into account any disease spreading among the civil population with which the soldiers come in contact and if necessary collaborate with civilian doctors in controlling diseases the spread of which may endanger the men under their care. Responsibility is increased in time of war since the risks are generally greater in territory where the fighting is going on or in occupied territory where disorganization of the health services and medical supplies may have taken place. Under such circumstances care of the civilian population may even become of primary importance.

HASCHKE KLUNDER² records some observations on circumstances in the Southern Ukraine during a period of German occupation from August to November 1942 which necessitated measures to control rabies and to treat persons who had been bitten by or had been in contact with infected animals. The first incident in August 1942 was the arrival of a woman with her five children in the local disease control centre from a village some distance away. These children had been bitten by a dog. The dog had been killed and the woman brought the carcass with her. The Russian veterinary investigation officer of the institute of this State reported the finding of Negri bodies in the *Cornu Ammonis* of the brain of this animal. The first measures taken were to order the shooting of all dogs in the village and a decree was issued to control dogs in the region. Vaccine was procured from a Russian State Bacteriological Institute to treat people who had been bitten. Nine weeks later the disease was introduced again into the same village by a rabid stray cat from another locality.

During the two outbreaks 54 people were vaccinated. 31 of these had been bitten by infected animals and 23 adults and children were treated prophylactically since they had been tending playing with or otherwise in contact with rabid animals either during the incubative stages or subsequently. Some of the latter group had been contaminated with saliva or blood during the process of killing the animals. The existence of the disease in the animals concerned was confirmed by controlled clinical observations or by laboratory diagnostic methods. The Russian vaccine furnished was prepared according to Phillips's method [see PHILLIPS *J. Immunology* 1922 v 7 409 the brains of rabies infected rabbits are ground up and quanta of 0.1 cc. of pure glycerin added to each 15 mgm. of brain tissue. This glycerinated suspension is stored at -2°C in an atmosphere freed of water and oxygen by the use of pyrogalllic acid and caustic potash. The virus suspension will retain its activity for several months. At the time of use 0.5 per cent carbolyzed saline is added in the proportion of 2 cc. to each 0.1 cc. of glycerinated virus suspension]. The doses of the vaccine injected and the duration of the treatment 10 to 40 days were determined by the degree of risk to which the patients had been subjected viz the site extent and severity of the bites and in the case of unbiten persons whether some contamination with saliva had taken place and whether predisposing factors such as skin lesions existed. Vaccine treatment was

² HASCHKE KLUNDER R. Berichte ueber allgemeine Arztliche Beobachtungen und Ergebnisse im Kriege und im Frieden. Zur Lyssa Abwehr in der Ukraine. *Deut. Militaerarz.* 1944 Feb. v 8 No 2 105-11 [18 refs.]

commenced in some cases as early as the first day after the bite and in the majority the first injection had been given within the 8 days after the bite of or contact with, a diseased animal. Exceptions were 9 9 11 and 16 days after bite or contact. In 40 cases the rabid animal was a dog in 7 a cat in 4 a cow and in 3 a calf. Two tables are given which summarize the information on the treated cases. No serious complications were recorded as a result from the vaccination, but a red-haired maid developed fever and urticaria after the 4th injection of vaccine. With the permission of the parents treatment was not discontinued and calcium was administered, the fever subsided and the allergic symptoms disappeared. In general, the vaccination treatment produced no reactions but on the appearance of the least signs of reaction a hot poultice was applied as a relief. During the period of occupation of the State from 1842 to 15 11 42, no cases of rabies in man were recorded and the last information, received on 15.3.43 was that no human cases had been reported up till then.

The author points out that he had the advantage of the assistance of the Russian civilian doctors and officials, who were accustomed to deal with such situations as outbreaks of rabies and possessed knowledge of handling rabies infection which the German sanitary officers did not have. In view of the fact that rabies is a more serious problem in Russia than in Germany each large state has a Hygiene and Bacteriology Institute which can deal with the problems of immunization etc. whereas in Germany the vaccination arrangements are not decentralized to the same extent.

The effectiveness of the control of rabies is dependent, as the author points out on the rapidity and thoroughness of the precautions taken such as quarantine measures for observing suspected animals for diagnostic purposes destruction and banning of dogs and vaccination of bitten persons.

III. Post Vaccinal Paralysis

THOMAS² describes a case of acute ascending paralysis (Landry) which developed on the date of the 14th daily injection with rabies vaccine the type of which is not stated. The patient had been bitten on the right hand by a dog thought to be rabid, and the wound was slight. There was no reaction following the first injection, but the patient, who came under the care of the author two days after the last injection, when paralysis had set in, stated that there was considerable burning redness and itching at the site of the second injection. This type of reaction occurred after all subsequent injections except the last three of the series. The history of the case is described in detail. Incidentally the family history was negative for allergic conditions as well as for mental or nervous disorders diabetes or other familial diseases. The paralysis ultimately affected the legs arms trunk, back and neck. A year from the onset of paralysis muscle strength had improved, although there was still slight foot drop and weakness in the hand grip but reflexes were fully active.

The treatment applied is stated to have a "scientific basis" and to be harmless but the author is not convinced that there was any value in the methods of treatment employed or that recovery would not have taken place without treatment. The treatment was the application of a modified type of the Kenny treatment, by a physiotherapist who had been trained in this method.¹ (This treatment has been used for paralyzed muscles in poliomyelitis and is not the orthodox method for such cases.) Thiamin hydrochloride was administered intravenously orally and later intramuscularly since it is stated to be beneficial in neurological disorders including poliomyelitis.

² THOMAS, C. R. Complications following Use of Antirabies Vaccine with Suggestions as to Treatment. *Southern Med. J.* 1944 Oct., v 37 No. 10 630-43. [15 refs.]

The author has apparently been particularly impressed by an article by HORACK [this *Bulletin* 1939 v 36 730] who considered allergy to be a factor in the development of reactions to antirabic treatment since he expresses the opinion that 'a review of the literature reveals an ever increasing amount of evidence in favour of an allergic basis for the development of complications following the use of antirabies vaccine. He suggests as did Horack that

all patients should be tested for sensitivity and if found to be sensitive should be desensitized before starting treatment. [There are cases of paralysis (*vide infra*) which have been recorded in which no special sensitivity to the antirabies vaccine was noticed during the course of the injections.] The wife of this patient described by Thomas had been bitten by the same dog and she had undergone the same course of vaccine treatment and no unfavourable results were recorded.

IMRIE⁴ points out that neurological complications following vaccination against rabies are fortunately rare but when they do occur they may be particularly distressing. He describes a case of paraplegia following antirabies vaccination. The patient was an officer who had been bitten by a stray dog while in a city of the Middle East. The dog also bit several other people and was presumably affected with rabies. Vaccination was commenced immediately and 15 daily injections of 10 cc of killed phenolized vaccine were given. There was some local discomfort at the site but no immediate ill effects were observed. Twenty days after the dog bite and the commencement of treatment the patient had pains in the shins and lumbar region which were believed to be rheumatic and were not severe. Twenty nine days after the completion of the vaccine treatment serious paralysis set in which gradually progressed and could be classified as of the dorso-lumbar type. The condition had greatly improved nine months later but there was still weakness in the gluteal and lower abdominal muscles though bladder and bowel function had returned. Re-education of the ataxic muscles was commenced at an early stage at first by simple exercises in bed later by increasingly complicated movements and finally by lessons in walking. It is stated that much more recovery seems unlikely and the improvement observed up to the time of writing the report had been largely due to the excellent mental attitude of the patient and the re-education of the muscles.

iv Miscellaneous

REMLINGER and BAILLY⁵ report that they have compared the immunizing power of street virus and fixed virus against the extremely severe test of intracerebral inoculation and that their results had shown them that the vaccinating power of the first is *nil* while in the case of the second on the contrary a real vaccinating action although in truth not very intense was observed. [The reviewer has so far been unable to procure the report of the protocols of the experiments.]

In view of this observation and taking into account some other differential characteristics between street and fixed virus the authors make the tentative suggestion that there may be some difference in antigenic structure between the two analogous to but not of necessity identical with that existing between rough and smooth strains of bacteria.

[Some 40 references to this complication of vaccination against rabies are given in this *Bulletin* between 1927 and 1936 and a particularly instructive table in 1928 v 25 pp 198-9.]

⁴ IMRIE A. H. A Case of Paraplegia following Anti-Rabies Vaccination. *J. Roy Army Med Corps* 1944 Oct v 83 No. 4 168-8

⁵ REMLINGER P & BAILLY J. Le virus rabique fixe est il smooth et le virus de rue rough? *Arch Inst Pasteur d'Algérie* 1943 Mar v 21 No 1 12-14

REMINGER and BAILLY⁴ make some comments on the investigations on rabies which have been carried out in America, especially during the last decade. They stress the fact that from reports appearing there the position with regard to the control of rabies and to the results obtained in the vaccination of man were far from satisfactory at the time the investigations were commenced. [There are many workers in America who still consider the position to be none too good. One of the hindrances appears to be lack of legislative measures which would ensure uniformity in methods of control.] Many important advances have been made in different centres but the authors refer particularly to the research work carried out at the Rockefeller Institute. They have been able to confirm the usefulness of the white mouse for diagnostic purposes in the way advocated by the American workers. They believe however that there are limitations to its usefulness. They are not yet convinced that it is the best animal to use for immunity experiments. [They will perhaps change their opinion when they have had an opportunity of reconsidering the evidence on the use of the mouse-potency test in assessing the value of vaccines. It must be pointed out that the results of immunity experiments with rabies carried out in America, in mice and in dogs have run in parallel. As already pointed out in a previous review it is just possible that if the same care was taken in selecting the rabbits e.g. with regard to age and breed, for immunity experiments the results obtained in these animals would run parallel with those in mice and dogs. Surely Reminger and Bailly must agree that methods of estimating the potency of the virus used for making a vaccine and also the potency of the immunizing agent are desirable. Even if in actual fact a vaccine which showed up badly in a mouse-potency test might still give some measure of protection when used in man it would appear to be preferable to use a product which gives a high degree of protection in mouse-potency tests. The use of the mouse has the advantage that it is a cheaper experimental animal than the dog, rabbit or monkey. This enables statistical evidence to be accumulated more easily.]

The present authors apparently feel that some of the earlier work on rabies has been treated somewhat cavalierly by some American authors but this can no doubt be explained by an overwhelming desire to advance. They themselves point out that Pasteur himself said: *la Science ne progresse qu'à condition de se détruire tous les 25 ans* and their appreciation of the investigations on rabies carried out by the American workers is confirmed by their suggestion that the rendezvous for a second International Conference on Rabies should be New York the first having been held in Paris in 1927. *Jan. 4 Gallows.*

MALARIA

PEREZ GARCERAN, D. E. Contribución al estudio de la influencia del sexo y la edad en la adquisición de infección palúdica. [Influence of Sex and Age in the Acquisition of Malaria Infection.] *Rev. Sanidad e Hig. Pública.* Madrid 1944 May-June v. 18, No. 3 207-18 1 chart.

Abundant statistical material available in the Provincial Health Institute of Cáceres in Spain has been used by the author to study the influence of the civil war on malaria incidence in his Province. To this end the age and sex distribution of malaria cases diagnosed by the dispensaries directly dependent upon the Central Antimalaria Commission about 60 in number as well as by Municipal

REMINGER, P. & BAILLY. J. Remarques au sujet des travaux de l'Institut Rockefeller relatifs à la rage. *Arch. Inst. Pasteur d'Algérie* 1943 Mar., v. 21 No. 1 15-25 [27 refs.]

dispensaries during the five year period 1931-35 is compared with that of the quinquennium 1936-40. The figures show but little change in malaria endemicity. The population figures used are those of the 1920 census.

Malaria is most frequent in the age group 1-4 followed by the groups 5-9 under 1 and 10-14 thereafter the incidence steadily declines. At all age groups except that of 60 and over the male incidence is significantly greater than the female. The difference is greatest in the groups 10-14 and 15-19. The author does not believe that greater risk of infection can explain the greater male susceptibility. In the early years of life the environment of the two sexes is identical. He believes that enhanced susceptibility or resistance is an attribute of sex.

Norman White

PEREZ PÉREZ Y PALAU F. Evolución y estado actual de la endemia palúdica en el Delta del Ebro y provincia de Tarragona. [Evolution and Present State of Endemic Malaria in the Ebro Delta and the Province of Tarragona.] *Rev Sanidad Hig Pública* Madrid 1944 Jan.-Feb v 18 No 1 52-74 8 figs [15 refs]

The Ebro Delta till 1937 suffered little from malaria in spite of very intense anophelism for which some 14 000 hectares of rice fields and market gardens were responsible [see this *Bulletin* 1933 v 30 63]. The only *Anopheles* found are *A. maculipennis maculipennis* and *A. maculipennis atroparvus* the former being the most abundant. Both are very markedly zoophilic in the Delta. In 1930 the spleen rate was only 8. The disturbances caused by the civil war were followed by a marked increase in the malaria endemicity of the Delta which increase is described in the present paper. Of the three antimalaria dispensaries in the region at San Jaime de Enveja Amposta and La Cava the first named has worked most consistently and has the most complete records. In 1926 430 malaria patients were seen in the dispensary of San Jaime parasites were found in 197 comprising 124 *P. vivax* 59 *P. malariae* and 14 *P. falciparum*. Thereafter the numbers declined year by year till 1937 when only 64 malaria patients were seen in 32 of whom parasites were found all *P. vivax*. In 1938 malaria incidence increased and a relatively high prevalence continued each year till 1942 when parasites were found in 1 070 of 1 789 cases of which 7 were *P. falciparum* the remainder *P. vivax* infections. The population served by the San Jaime dispensary is only about 3 500. No *P. malariae* infection has been found in this dispensary since 1931 and no *P. falciparum* between 1930 and 1942 when it reappeared. The total number of patients seen in the three dispensaries in 1942 was 4 804 in 3 565 of whom parasites were found. The total population of the area is about 20 000.

Relatively large migratory labour forces engaged in the rice fields in planting time and harvest provide facilities for the transfer of malaria infection to other parts of the country. This fact endows the malaria problem of the Delta with more than local importance. Elsewhere in the Province malaria endemicity is low and its control presents little difficulty.

In the conditions pertaining in the Delta anti mosquito measures are hardly practicable. Reliance is placed on the early and thorough treatment of cases and the prophylactic use of anti malarial drugs in certain places. Notable improvement was effected in the antimalaria service in 1943 and there was a corresponding improvement in the endemic situation.

Norman White

COLLIGNON. Zones paludéennes en Algérie et principes généraux de la prophylaxie. [Malaria in Algeria. General Principles of Prophylaxis.] *Bull Office Internat d'Hyg Publique* 1942, Apr-May-June v 34 Nos. 4-5-6 129-30 1 map

LOIRENTU. Le paludisme en Afrique Equatoriale Française. [Malaria in French Equatorial Africa.] *Bull. Office Internat. d'Hyg. Publique* 1942, Jan.-Feb.-Mar. \ 34 Nos. 1-3-3 24-51 1 map

BOURGUIGNON, G. C. Le problème du paludisme dans la région d'Elisabethville. [The Malaria Problem in the Elisabethville Region.] *Rec. Trav. Sci. Méd. Congo Bidge Léopoldville* 1944 Jan. \ 2 165-203 10 graphs.

The main part of this paper is concerned with the results of the examination of blood smears from both Europeans and natives sent to the laboratory during a period of 9 years for confirmation of the diagnosis of malaria which clinical symptoms had suggested. The total number of such examinations was 38 490. In the case of Europeans the number of positive findings is a very close approximation to the total incidence of malaria in Elisabethville. For the natives the figures are merely indicative of active malaria infection in a population heavily parasitized.

Climatic and malarial conditions are very different in the high Katanga plateau on which Elisabethville is situated from those prevailing in the central Congo basin. In Elisabethville there is a very well marked cold season with temperatures falling to freezing point followed, about the beginning of November by an equally well-marked rainy season. The rainy season continues till the end of March, with a remission at the end of January. The European part of Elisabethville is well separated from the native town, but as the majority of European households employ at least one or two native servants, who spend some hours each day in the native city the segregation is not complete.

Graphs are produced showing the monthly incidence of positive malaria findings for Europeans and natives respectively in each of the nine years. There is a remarkable similarity between the curves of the different years. Each year malaria among Europeans is at its lowest ebb sometimes almost absent in the cold weather months July, August and September. Clinically active native malaria is similarly lowest at this season but some cases continue to occur. From October onwards cases become progressively more numerous though there may be no very marked rise in the European curve until February. The maximum incidence of native cases is generally in April—the maximum European incidence comes at least a month later.

Anopheles gambiae *f. fuscus* and *f. maculipalpis* appear to be important vectors of malaria in Elisabethville. *P. falciparum* is responsible for practically all the malaria. *P. malariae* is occasionally found in young native children but extremely rarely in Europeans. *P. mex* has never been found except in native children under two years of age and *P. olex* has been seen only once. The gametocyte indices are surprisingly low—much lower than elsewhere in the Congo.

The trophozoites of *P. falciparum* in Elisabethville are for the most part characterized by their extremely small size—especially among the Europeans they resemble *P. leue* described by STREPTZ. Among the natives these small forms predominate in the cold season—with the advent of the rains and the concomitant increase in clinical manifestations of malaria the usual larger forms of trophozoites reappear. It would seem that the climate altitude or seasonal anophelism is of a nature to influence the size of the trophozoites.

The paper contains the results of the blood examination of four groups of villagers in this south-eastern corner of the Congo—carried out in August toward the close of the cold season. The percentage of positive malaria findings was 68.6 as compared with 50 for Elisabethville.

Norman White

WATSON R. B. & RICE Margaret E. Some Epidemiological Characteristics of Malaria in North Alabama as determined by Data collected over the Twenty-Year Period 1923-1942. *Amer J Hyg* 1944 Sept. v 40 No 2 199-208 5 figs

Early in 1923 branch laboratories were established at Huntsville and Decatur to provide a diagnostic service for doctors practising in north Alabama. During 20 years these laboratories have examined 58 608 blood films 82 per cent. of them from Morgan and Madison Counties in which the laboratories are situated. Thin films only were examined till 1933 in Decatur and 1938 in Huntsville. Since then thick films have been examined as a routine.

Routine collections of *A. quadrimaculatus* were begun in 1935 from approximately 150 collecting stations. Catches were made bi weekly before the impoundage of Wheeler Lake and weekly thereafter from May to October both inclusive each year.

The percentage positive blood film findings are not strictly comparable. In the early years most of the films were from patients with fever. Later doctors took films as a routine from all new patients and some industrial plants require all new employees to be examined for malaria. But the figures show the trend of malaria incidence throughout the 20-year period and through each of those years.

Unusually severe outbreaks of malaria were experienced in 1923, 1929 and 1934, since 1934 the prevalence has decreased consistently. In 1923 the excessive prevalence was due almost entirely to *P. falciparum*, in all of the subsequent years *P. vivax* infections have been preponderant. *P. malariae* was found only three times during the 20 years.

Malaria incidence shows a marked rise from July to October, the month of maximum prevalence. The increase concerns both *P. vivax* and *P. falciparum* infections, but the former preponderates in every month. From February to May there is an increase in *P. vivax* infection rates due to relapse of infections acquired some 7 months previously. *P. falciparum* infection rates decline during this period. There is a slight but well marked decline of malaria incidence in June. The period of malaria transmission commences in June, the earliest date on which sporozoites have been found in mosquitoes was May 16th. In general the highest seasonal level for anophelism was followed 30 to 60 days later by the highest malaria rate for the year. In certain areas anophelism has declined but there are other areas in the Tennessee Valley in which the production of *A. quadrimaculatus* has been most prolific, notably in 1941 and 1942. In spite of this there has been a rapid decline in malaria rates even in areas of excessive anophelism. Mosquito-proofing of houses may account for this in many places, but a decline has also been noted in places where no mosquito proofing has been done. It must be pointed out however that the statistical material used for the determination of infection rates hardly justifies dogmatic statements about fluctuations of malaria incidence from year to year.

Norman White

ETHERINGTON D. Fertilization of *A. maculipennis* var. *labranchiae* in the Laboratory [Correspondence.] *Nature* 1944 Nov. 11 608

Anopheles maculipennis var. *labranchiae* will swarm in a cage one metre high and fifty centimetres wide if a blue light of intensity 3 f.c. at 30 cm. is placed above the cage. It has also been carried completely round the life-cycle in a cage rather dimly illuminated from a window.

P. A. Buxton

CORREIA, R. R. & RAMOS A. S. Os anofelinos da Ilha de Santo Amaro. [Anophelines of the Island of Santo Amaro.] *Arquivos de Hyg e Saúde Pública*, São Paulo 1944 Sept. v 9 No 22, 9-18 2 figs. [11 refs.] English summary

STOHLMAST, H. Malariaübertragung auf Blutspender (Transmission of Malaria to Blood Donors during Direct Transfusions.) *Wösch. med. Woch.* 1943 Jan. 29 v 90 No 5, 84-5.

Of five persons who gave transfusions to a soldier infected with benign tertian malaria, three (two certainly and one probably) developed the disease. None of these three donors had been outside Germany. In the two cases in which observations could be made the incubation period was 17 and 18 days respectively. The transfusions were given directly from donor to patient by means of Beck's apparatus which is essentially a form of two-way syringe. Evidently there was some reflux of blood from the recipient to the donor.

(Direct transfusion is at present so little used that emphasis on the necessity of using an apparatus that makes impossible any reflux of blood from recipient to donor is not of very general interest. However any information about the transmission of malaria by transfusion is of value because the spread of this infection from donor to recipient is likely to become increasingly common in the next few years. It has been shown to occur even when the donor's blood is stored for some days (this *Bulletin* 1942, v 39 252.)

P. L. Madison.

SOBERÓN Y PARRA, G. Intradermo-reacción que puede ser útil en el diagnóstico del paludismo (Intradermal Reaction for the Diagnosis of Malaria.) *Rev. Med. Trop. y Parasit. Habana* 1944 Mar-Apr v 10 No 2, 26-8 1 fig.

The author describes an intradermal test for the diagnosis of malaria, which he considers may be of use in cases in which no parasites are found in the peripheral blood, for doctors in places in which there are no laboratory facilities for the control of treatment and in large-scale inquiries.

The reagent is made from the blood of a fowl very heavily parasitized with *Plasmodium gallinaceum*. Full details are given of the technique employed in the manufacture of the antigen, a technique which the author admits is capable of improvement. The intradermal injection of 1/10 cc. of the antigen, in the absence of malaria, is followed by an inflammatory reaction covering an area of one to one and a half centimetres in diameter which reaches its maximum intensity in 8-12 hours thereafter it subsides and disappears in most cases within 24 hours. The absence of such reaction indicates malaria infection. In 242 cases of malaria verified by blood examination the test was indicative of such infection in 227 (93.8 per cent.). The test was applied to 837 patients suffering from a great variety of conditions. Cancer patients gave the most anomalous results. 31 of 129 being positive. Norman White.

BOYD M. F. & KITCHEN S. F. Renewed Clinical Activity in Naturally Induced Virax Malaria. *Amer. J. Trop. Med.* 1944 July v 24 No. 4 221-34 1 fig.

During ten years 358 white patients were successfully inoculated with virax malaria by mosquitoes in the malaria therapy service of the Florida State Hospital. Of these 375 experienced attacks of clinical malaria. Assuming that remissions of 5 or more days marked the end of the primary attack, 40.2 per cent. of 261 patients with spontaneous remissions, and 51.8 per cent. of 114 patients in whom remissions were induced by drugs, exhibited secondary clinical activity. No such renewed clinical activity was seen in patients whose primary attack exceeded 55 days or 43 days before interruption by medication. After spontaneous remission 46.5 per cent. of the patients who received no subsequent therapy exhibited renewed clinical activity after induced remission the corresponding percentage was 73.0. None of 30 spontaneous remissions was

followed by secondary attacks when full therapy was given. Eight of 37 patients whose remissions were induced had secondary attacks in spite of full therapy. Full therapy means the administration of 14 gm or more of quinine or of 1.5 gm of atabrin in divided doses. When the effect of treatment is the production of remission only the duration of the remission tends to vary directly with the quantity of antimalarial drug given.

Few of the spontaneous remissions exceeded three weeks the longest was 62 days the mean duration being 11.1 days. The earliest secondary activity rarely exceeded three weeks the mean duration being 8.9 days. The mean duration of induced remissions was 60.4 days and of the subsequent clinical attack 7.7 days.

Most *vivax* infected patients have quotidian intermittent paroxysms due to successive and alternating maturation of two broods of parasites. It is suggested that remissions whose length is in odd-numbered days are terminated by the reactivation of the parasite brood the suppression of which produced it. Remissions of 81 days or less were more frequently of an odd number of days in duration the duration of longer remissions was more frequently of an even number of days.

Some of the attacks which terminated spontaneously were milder than those which were interrupted—a lower proportion were quotidian throughout. On reactivation however tertian fever was more commonly found in patients whose first remission had been induced by drugs the drugs had not been equally deleterious to both broods of parasites.

The onsets of the renewal of clinical activity exhibit two frequency distributions. One is common to both spontaneous and induced remission cases. Here renewed activity of the primary parasitaemia may occur as long as 174 days after inoculation. Remissions occurring within this range of time do not mark the presumptive termination of the primary parasitaemia and the attacks might well be termed recrudescences. On the other hand activity observed only after therapeutic interference arising after the 204th day is probably not related to the primary parasitaemia it might be aptly termed relapse.

Norman White

BOYD M. F. On the Parasite Density prevailing at certain Periods in *Vivax* Malaria Infections. *J Nat Malaria Soc* Tallahassee Fla 1944 Sept v 3 No 3 159-67

This study is based on observations made on 307 adult white patients with naturally induced *vivax* malaria. The parasite density on the day of onset the first day with temperature of 100°F varied considerably. In 16.9 per cent of the patients no parasites were detected in the peripheral blood on the day of onset in 81.2 per cent. the parasites did not exceed 100 per cmm. in 7.2 per cent the parasite density exceeded 1 000 per cmm. None of the onsets occurring within 14 days of inoculation had parasite densities exceeding 500 per cmm. all onsets occurring more than 20 days after inoculation were accompanied by parasite densities of 10 to 10 000 per cmm. The parasite density at onset increased as the interval between the end of the prepatent period and the onset increased.

Sixty per cent of the patients had parasite densities exceeding 1 000 per cmm. when the temperature first reached 104°F. The longer after inoculation this event occurred the higher the coincident parasitaemia.

Clinical activity usually terminated spontaneously with a parasite density of 1 001-5 000 per cmm. In some patients however the terminal density was lower than that which initiated the attack. The density on recrudescence or relapse was generally higher than it was at the primary onset but in some cases

the density was substantially the same or even lower. The densities did not appear to become progressively higher with later reactivations.

Norman White

APPLEBAUM I L. & SHRAGER, J. Pneumonitis associated with Malaria. *Arch Intern Med.* 1944 Sept. v 74 No 3 155-62, 5 figs. [21 refs.]

This paper starts with references to the extensive literature on the association of malaria with pneumonia, and to the undecided question whether or not there is a malarial pneumonia. The authors report observations upon 125 consecutive patients with pneumonia associated with malaria, who were admitted to the Gorgas Hospital, Panama, between January 1942 and May 1943. Seventy per cent of the patients were white men of military age. Among such men the incidence of pneumonia associated with malaria was 3.7 per cent of the incidence of uncomplicated malaria. The cases were most numerous during the rainy season when both malaria and pneumonia are most prevalent. *P. vivax* and *P. falciparum* infections were associated with pneumonia to about the same extent. X-ray examination showed that the lower lobes of the lung were most commonly affected and that the lesions were of the lobular type. The combined disease was not severe. The average stay in hospital was 17½ days, only slightly longer than that for uncomplicated pneumonia or malaria. There was only one death; this was caused by cerebral malaria and the pneumonia was not thought to have contributed to the fatal issue. One group of cases responded to sulphona-mide compounds. In 39 of 50 patients the pneumonia yielded to the administration of antimalarial drugs alone. Some cases showed an inadequate response to both forms of treatment but ran a self-limited course. The sputum of 62 patients was examined; in 55 no pathogenic organisms were isolated. Pneumococci were found in 5 haemolytic streptococci in one, and *Staphylococcus aureus* in one.

Norman White.

HARRISON K. S. & DAKIN W. P. H. Nephrotic Type of Nephritis in association with Quartan Malaria. *Med J Australia* 1944 July 22, v 2, No. 4 80

A female native child five years of age was admitted to hospital in a south Pacific island with oedema of legs, vulva and lower part of back; ascites and puffiness of face and eyelids. The spleen extended two inches below the costal margin. There was a small pleural effusion at the base of each lung. When the scanty urine was boiled, three-quarters of its volume was albumin. There were numerous granular, cellular and hyaline casts and a few red blood cells.

Plasmodium malariae was found in the blood. There were numerous hookworm ova in the faeces. Antimalarial treatment, quinine atebem and plasmoquine in succession, caused the disappearance of the more acute symptoms. Then the hookworm infection was treated with carbon tetrachloride. Convalescence was complicated by a secondary yaws eruption which yielded rapidly to mapharsen, after which the patient contracted influenza pneumonia which responded to sulphathiazole. The patient eventually recovered. It is not certain that quartan malaria was responsible for the nephrosis in this case, but the association of the two conditions has been reported from many places though not hitherto the authors believe from the south west Pacific.

Norman White

MAXSON BARR, P. The Nature and Treatment of War Time Malaria Relapses in England. *Med Press & Circular* 1944 Nov. 29 342-7

Malaria relapses among troops returned from Africa and Mediterranean countries are occurring in many parts of Britain. To many practitioners these

cases present novel problems and this article was written for their benefit. The multiplicity of malaria treatments recommended is often a source of confusion. A table outlines in schematic form 26 such treatments. A description is given of the chief characteristics of benign tertian and malignant tertian malaria. Relapses of the former will be most frequent in this country.

For cases where quinine is to be given intramuscularly, a new preparation *solvochin* is considered superior to other preparations. *Solvochin* is a 25 per cent solution of quinine in phenyldimethyl pyrazolon. Its reaction is alkaline pH 7.2. It causes no local irritation. The recommended dose 2.2 cc contains 0.5 gm (7½ grains) of quinine. The treatments advised are —

Benign tertian severe cases with numerous parasites — two intramuscular injections of 2.2 cc *solvochin* daily for two days. 30 grains quinine hydrochloride daily by mouth for the next two days then 20 grains quinine hydrochloride by mouth daily for five days. In less severe cases the intramuscular injections can be omitted. This treatment of the acute attack is followed by suppressive anti-relapse treatment consisting of pamaquin 0.04 gm and 7½ grains of quinine daily for seven days which course should be repeated after four days interval. If well tolerated four or five such suppressive courses can be given.

Malignant tertian severe infections with numerous parasites — two intramuscular injections of *solvochin* 2.2 cc daily for four days then mepacrine 0.1 gm, and quinine hydrochloride 10 grains thrice daily for seven days. After five days interval the mepacrine and quinine course should be repeated. Two further mepacrine and quinine courses at weekly intervals are recommended for anti-relapse treatment. In less severe cases the intramuscular treatment is not necessary.

Norman White

Rico B C La Calgliquina Sandoz en el tratamiento del paludismo
["Calgliquina" Sandoz in the Treatment of Malaria.] *Medicina Mexico*
1944 Aug 10 v 24 No 465 317-21

Calgliquina Sandoz is gluconate of quinine in a solution of gluconolactate-gluconate of calcium. 10 cc. contain 0.6 gm of quinine gluconate. Its pH is 7. On intramuscular injection it causes none of the severe local reactions associated with most quinine preparations and the quinine is completely absorbed. It is a safe preparation for intravenous administration. The calcium inhibits anaphylactic shock and increases the tolerance of the organism for quinine. It also reactivates chronic infections rendering the parasites accessible to the quinine. The preparation has cardio-tonic properties. For the treatment of acute attacks in adults two intravenous injections a day each of 5 cc are recommended for chronic cases 5 cc a day intravenously. In acute cases the treatment can be continued for 8 to 10 days. Intramuscular injections are recommended for children in diminished doses according to age. The author has noted no toxic effects from the use of *Calgliquina* and has found it to be of great value in cases that failed to respond to other antimalarial drugs. He describes four chronic and one acute case of malaria which were successfully treated with intravenous *Calgliquina*.

Norman White

DAS GUPTA B M. SIDDONS L. B & CHAKRAVARTI H. Quinine and *Astonia scholaris* (Chhatim) in Malaria. A Study of possible Synergy. *Indian Med Gaz* 1944 Sept. v 79 No 9 408-14 2 charts

Recent work has discounted the former belief that the alkaloids contained in the bark of *Astonia scholaris* (chhatim) were of value in the treatment of malaria. The present report gives no support to the view that chhatim given in

combination with quinine enhances the antimalarial activity of the latter drug. Seventeen patients suffering from malaria were the subjects of the investigation. They were all adult or adolescent male Bengalees. There were two *P. malariae* infections, the remainder were *P. falciparum* or *P. vivax* or both, ten being mixed infections. Most of the cases were of several weeks' duration, that is to say low grade residual infections such as are commonly seen at the end of the transmission season. Eight patients were treated with two grains of quinine sulphate thrice daily for six days. Nine patients received the same doses of quinine reinforced with 12 grains of powdered bark of *Alstonia scholaris* thrice daily for six days. There was no significant difference between the results obtained in the two groups. These very small doses of quinine controlled both fever and parasites in most cases but relapses after short intervals were the rule. The conclusion is that such small doses are not justified—they would be dangerous in early *P. falciparum* infections. *Norman White*

BRAHMACHARI U. Berberine in Malaria. A Preliminary Note. *Indian Med Gaz* 1944 June, v 79 No 6 259

The author states that berberine sulphate has the property of driving malaria parasites from the internal organs into the peripheral circulation where they can be readily attacked by quinine. This observation he ascribes to CHOPRA. It is contended that berberine sulphate should be a valuable adjuvant to quinine in the treatment of malaria. Its toxicity is low and it can be safely administered intravenously. No clinical observations are produced in support of the suggestion. [See also this *Bulletin* 1933 v 30 42] *Norman White*

HIATT E. P. Plasma Concentrations following the Oral Administration of Single Doses of the Principal Alkaloids of Cinchona Bark. *J Pharm & Exper Therap* 1944 June v 81 No 2, 160-63 2 figs.

The alkaloids were given orally to healthy volunteers three hours after breakfast the dose being 10 mgm of free base per kgm body weight i.e. 0.6 gm. or about 10 grains for a 9½ stone man. The concentration of the different alkaloids in the plasma of the individual volunteers is shown in a series of graphs. There was considerable variation between different individuals but the peak was usually reached after 2-3 hours. For quinine the average value was about 3 mgm per litre for quinidine about 2 mgm, for cinchonidine about 2.5 mgm and for cinchonine about 0.5 mgm. After 24 hours the concentration of the first three alkaloids was about 0.2-0.8 mgm. per litre, while cinchonine could not be detected. If totaquina (L.S.P.) was given (3 subjects) the concentration of total alkaloids in the blood showed an average value comparable with those of the individual alkaloids. *F. Hocking*

SIEGEL H. & MUSHETT C. W. Structural Changes following Administration of Quinaerine Hydrochloride. *Arch Pathology* 1944 Aug v 38 No 2, 63-70 5 figs. (13 refs)

Pathological results of quinaerine treatment have been described in papers abstracted in this *Bulletin* 1934 v 31 171 and 1944 v 41 99 and 649. The present investigation is part of a general study of the effects of quinaerine (atebrin dihydrochloride) in experimental animals in which 25 dogs, 20 monkeys, 50 chickens, 20 hamsters, 20 guinea-pigs, 20 rabbits and 400 rats were used. All the animals received an adequate diet without stint and were housed in good conditions. The drug was administered in 3 per cent. solution by stomach tube, the doses given being calculated as a percentage of the LD50 which is

900 mg per kilo for rats. The tissues for examination were generally fixed in formalin and stained with Delafield's haematoxylin and eosin but other methods of fixing and staining were sometimes employed. The rat was found to be the most suitable animal for demonstrating in a general way the tissue changes which occur as the result of treatment with quinacrine and detailed descriptions of the results are given for this animal but cannot be fully abstracted.

After a single LD50 a basophilic substance was present in cells of the reticulo-endothelial system and in certain parenchymatous cells. It was shown to be quinacrine or some closely related substance. Large areas of the liver as well as smaller foci showed coagulative necrosis generally accompanied by only slight inflammatory reaction. From 4 to 8 weeks after recovery from this dosage the rats appeared to be in normal health but the livers of some had depressed scars mostly of the right lobe and were adherent to adjacent structures. The fact that this lobe was chiefly affected was shown by analysis not to be due to a greater concentration of the drug at that site. After the same period following smaller doses the changes in the liver were no longer visible. In spite of the extensive liver damage sometimes encountered no evidence of a haemorrhagic diathesis was noted. Besides those in the liver pathological changes were found in the heart, adrenal gland, kidney, spleen, reticuloendothelial system, stomach and occasionally in striated muscle with lesser changes in other tissues after a single LD50. The outward appearance of the test animals as well as the accompanying histological changes in their tissues after smaller repeated doses are described. Massive haemoglobinuria was induced only in young rats receiving a particular dosage of drug and at times acute catarrhal enteritis and colitis occurred.

Deaths amongst animals receiving small doses of quinacrine over a long period were paralleled to some extent in the controls and it was not clear whether the drug rendered the animals more prone to natural infections which occurred mostly in the lungs. A brief description of results obtained with the animals other than rats is given. Myocardial lesions occurred only in hamsters while liver necrosis in dogs was rare.

J D Fulton

ROY NAV MED BULL. No 13 14-19
Suppressive Treatment (Chemoprophylaxis)
Dept BUMED News Letter Vol. 4 No 1]

Malaria—Recommendations for
[Reprinted from U.S. Navy

Suppressive treatment with atabrine [mepacrine] is recommended for naval personnel who are exposed to malarial infection. One tablet of 0.1 gm (1½ grains) should be taken daily at the evening meal. This routine should be continued throughout the period of exposure to infection and for a month afterwards if however there is a high incidence among the men this suppressive treatment should be continued while they are in the theatre of war whether based on a malarious or a non malarious area.

In some persons mepacrine causes nausea and vomiting or colic and diarrhoea but this is an initial intolerance often due to taking the drug on an empty stomach or in too large a dose. temporary reduction of the dose leads to tolerance and less than one per cent of persons are unable to continue taking it. The routine should be modified in certain circumstances when clinical attacks occur they are treated and the suppressive doses are resumed afterwards if the incidence of clinical attacks is high say after return from strenuous combat it may be reduced by increasing the daily suppressive dose to three tablets (0.3 gm.) daily after meals for 3-5 days and then returning to 0.1 gm. a day as before.

Suppressive treatment should be begun a month or two before arrival at a place where it will be required in other places different measures of control may have made suppressive treatment unnecessary so information about the area should be obtained beforehand.

A certain level of concentration of the drug in the blood is required before suppressive treatment becomes effective as the tissues have first to be saturated half the maximum concentration is reached in a week and the maximum in four weeks. In urgent circumstances of war it may be necessary to give 0.2 gm. daily for a week so as to establish a higher plane of concentration for a time as a safeguard against unavoidable irregular administration.

There is no evidence of toxicity from long continued dosage e.g. over a year and fears that it produces impotence or sterility are unfounded.

J. F. Corson

ROMERO MOLINER R. Profilaxis del paludismo tropical con atepe y con quinina. Resultados y critica. [Prophylaxis of Tropical Malaria with Atepe and with Quinine.] *Verd Colonial* Madrid 1944 June 1 v. 3 No. 6 368-72 2 graphs. [16 refs.]

A military detachment was stationed in small groups along an intensely malarious coast line of Fernando Po. Men suffering from malaria were treated in the military hospital at Concepción. The composition of the detachment was unchanged throughout the period of observation. The men from the date of their arrival in the colony were each given a daily dose of 0.4 gm. of quinine sulphate. From May 1943 onwards this quinine prophylaxis was closely supervised and is believed to have been complete in spite of which malaria incidence was high. The peak of the incidence curve was during the first ten days of August when 49 cases occurred. On the 10th August the quinine prophylaxis was replaced by atepe two tablets on each of two successive days each week. (A tablet of atepe contains atehrin 0.1 gm. and plasmoquine 0.005 gm. Thereafter there was a remarkably lowered incidence of malaria, which continued through September and October. This is the rainy season which is usually a most unhealthy period of the year. All the malaria in this area is due to *P. falciparum*.

Norman White

WHITE R. SENIOR & VENKAT RAO V. Regulation of the Control of Anopheles of the *flavistilis*-Group by Anti-Adult Spraying. *Indian Med Gaz* 1944 Aug. v. 79 No. 8, 364-9 1 fig.

The *flavistilis* group consists of *A. flavistilis*, *A. varuna* and *A. minimus*. All three species are potent malaria transmitters in India and *A. minimus* has a wide dispersion in Burma, Southern China and French Indo-China. The habits of adult *A. minimus* have been studied by Muirhead Thomson [this *Bulletin* 1942, v. 39 597 where other references are given]. He found that *A. minimus* takes two days to digest its blood meal in the hot monsoon season and lays its eggs on the second night after feeding in cold weather this period is increased to 4-6 days. Most *A. minimus* leave the house toward sundown there is no similar attraction towards light at dawn. There is a considerable daily turn-over of the *A. minimus* population in houses. About 90 per cent. of blood feeding takes place after midnight. After oviposition *A. minimus* returns for another blood meal on the same night. In fertilized females one blood meal is sufficient for egg laying.

The first-named author of the present paper has for two years been carrying out experiments to extend Thomson's work and to observe the effects of spraying on the numbers and behaviour of 8 species of *Anopheles* including all three

members of the *fluvialis*-group. These observations are not yet ready for publication but the findings in so far as they concern the control of *Anopheles* of the *fluvialis*-group by spraying are made available without delay in view of the shortage of supply of insecticidal sprays. He has found that in a house caught to emptiness daily 96 per cent of *A. fluvialis* and *A. varuna* and all *A. minimus* are fresh fed the next morning. If thus catching to emptiness be carried out hot once a week 82 per cent of *A. fluvialis* and *A. minimus* are fresh fed. The number of all three species found in empty houses is only from 11 to 15 per cent of the number found in inhabited houses. In a house occupied only by a cow the number of *A. fluvialis* is 16 per cent. of *A. minimus* 50 per cent and of *A. varuna* almost 100 per cent of their numbers found in a similar house with human bait. Most of the *A. varuna* caught near cattle 67 per cent were only resting there after a recent meal on human blood. Daily spraying reduces the number of old *fluvialis* and by 38 per cent in *A. varuna*. It halves the total numbers of *A. fluvialis* and *A. varuna* but reduces the number of old wings by only 27 per cent. Once a week spraying reduces the number of old wings by 66 per cent in *A. fluvialis* and by 38 per cent in *A. varuna*. (The numbers of old wing *A. minimus* captured were too small to apply this criterion.) The numbers of all three species found resting in houses sprayed once a week were actually greater than in exactly similar unsprayed houses. This curious phenomenon was not found with *A. culicifacies* in the same houses so is not explained by attractive oes of bait it is not understood.

There is in all three species an almost complete daily turnover of the individuals in a house. Insects which have fed one night have left the next Departures are not delayed by lowered temperatures though digestion is Individual mosquitoes are thus vulnerable to spraying for only one daylight period in each digestion-ovarian cycle.

The rationale of spray control is to destroy the mosquito before it becomes infective. Taking into account the length of the sporogony cycle this means that in the monsoon the mosquito must be destroyed before the 9th day in the autumn before the 10th day and in the cold weather before the 14th day. These periods vary of course in different localities. The authors suggest various spacing of spraying which will ensure that any given mosquito will run two chances of being hit before its glands become infected.

To illustrate the results of spraying six days a week the observations in Guwahati are quoted. Thirty sprayed railway quarters were compared with 30 adjacent unsprayed quarters. Figures for once weekly catches over 26 months for all three species were unsprayed quarters 1112 mosquitoes with oöcyst rate of 4.7 and sporozoite rate of 3.5. Sprayed quarters 46 mosquitoes with oöcyst rate of 4.3 and sporozoite rate of 2.2. The density was therefore reduced 24.1 and it is by this reduction that malaria control is achieved. In Posoita Smghbhum mosquito density was reduced 6.1 by intermittent spraying—2 days spray 2 days no spray 1 day spray 2 days no spray 2 days spray. This rhythm was repeated after 2 days no spray. In the cooler weather from mid-October onward when the digestion cycle is 72 hours the rhythm was changed to 3 days spray 4 days no spray and so on. In this station the incidence of malaria was but 2 per cent. higher than in previous years when daily sprayings were employed.

If daily spraying be done with kerosene alone there is a greater reduction in the number of mosquitoes caught than if daily spraying be done with pyrethrum kerosene mixture. It is not known whether the repellent action of kerosene prevents the entrance of mosquitoes to bite or only their remaining to rest after biting.

The conclusions arrived at apply only to the control of the *fluvialis*-group. *A. culicifacies* can be adequately controlled by weekly or at most bi-weekly spraying
Norman White

WASICKY R. & UNTI, O. Diclono-difenil triclono-etano (DDT) no combate às larvas de culicídeos. [Dichlor Diphenyl Trichloroethane (D.D.T.) In the Campaign against Mosquito Larvae.] *Arquivos de Hig. e Saúde Pública*. São Paulo. 1944 May v 9 No 21 89-102. English summary

The authors report on the value of DDT against mosquito larvae. The bulk of their work has been done with the material dispersed in colloidal form through the water (the method of dispersal not being stated)

Working in aquaria it is found that a dilution of 1/10 000 000 kills mosquito larvae in 30 to 60 minutes. 1/50 000 000 in 24 to 36 hours. No difference is recorded between larvae of *Anopheles albistarsis*, *A. stroderi* and *Culex*

A single application is effective in an aquarium for four months' death of larvae requiring a longer exposure as time passes. The material is not repellent to female mosquitoes and does not kill mosquito eggs

Large scale applications are described, e.g. a swimming bath which contained numerous larvae of five species of *Anopheles* and also *Culiscaes*. The surface was treated with a dosage corresponding to 1/25 000 000 throughout the bath and all larvae were killed none reappeared for twenty days

Experiments are briefly described in which the DDT is used as a larvicide in mineral oil, or absorbed on cork powder

A series of experiments are described in which DDT was administered by various routes to experimental animals of several sorts. The authors are convinced of its complete systemic toxicity. Ointments and colloidal solutions containing as much as 5 per cent do not cause irritation of skin or conjunctiva
P. A. Buxton

ROZENBOOM L. E. & HESS A. D. The Relation of the Intersection Line to the Production of *Anopheles quadrimaculatus*. *J. Nat. Malaria Soc.* Tallahassee Fla. 1944 Sept. v 9 No 3, 169-79 2 figs.

A. quadrimaculatus breeding is confined to waters containing vegetation and floatage. In determining the suitability of water for the production of this species the intersection line is of value. This is defined as "the line of intersection between three interfaces: water-air, water-plant and plant-air." "Intersection value" is the number of meters of intersection line per square meter of water surface.

A square wooden frame one-half meter on a side and about eight inches deep was used as the standard sampler. This was placed among the plants, and the collector standing above it looked down and estimated the percentage of the water surface that was covered by the vegetation and the amount of intersection line within the area enclosed by the frame. Except for lotus the amount of intersection line in each sample was recorded as high, medium, low or zero the latter group including some samples which contained a small amount of intersection line. In the case of *Ortus* absolute measurements were made with a flexible steel tape. Egg and larva collections were made by skimming the surface of the water within the frame with a cup.

Studies were made of eight species of littoral plants in the North Alabama section of the Tennessee Valley representing five ecological types: submerged, grass-like leafy-emergent, naked-emergent, and floating-leaved. It was found that with individual plant species there is a close positive correlation between the production of *A. quadrimaculatus* and the amount of intersection line per

unit of water surface area. The increased mosquito production which accompanies high intersection values is due to increased oviposition and decreased larval mortality. The only exception occurred in dense stands of *Eleocharis quadrangulata* a naked emergent type of plant which appeared to present a mechanical barrier to anopheline oviposition. *Norman White*

HESS A. D. & KIEER C. C. Water Level Management for Malaria Control on Impounded Waters. *J Nat Malaria Soc* Tallahassee Fla 1944 Sept v 3 No. 3 181-96 4 figs

This paper describes the water level management on impounded waters of the Tennessee Valley Authority with particular reference to malaria control. Such management is effective in so far as it secures a clean water surface which will not produce *A. quadrimaculatus*. Success demands attention to accessory measures including (1) proper reservoir preparation—reservoir clearance, marginal drainage and reconditioning of the zone of fluctuation, (2) winter time impoundage, (3) shoreline maintenance—annual shoreline conditioning, aquatic growth control, marginal grazing and drainage maintenance, (4) permanent shoreline improvement.

On the nine main river reservoirs of the Tennessee Valley Authority, water level management has regard to their three main purposes: navigation, flood control and the generation of hydro-electric power. Some time during the winter or early spring the water is brought up to the maximum flood surcharge level and is subsequently brought back to the normal maximum summertime level. This results in the stranding of drift and floatage which might otherwise favour mosquito breeding later on. It is important that water should not be left at the maximum flood surcharge level after the beginning of the spring growth period about April 1st in the lower valley, as it might kill timber in the uncleared zone and dead timber adds to the accumulation of drift and floatage. After the first half of May such flood water might cause uncontrollable breeding of *A. quadrimaculatus*.

A relatively constant water level at the normal maximum summer level is maintained from the period of early spring growth to the beginning of moderate *A. quadrimaculatus* production from about April 1st to almost the end of May; this period may be two weeks or so later in the northern part of the area. This constant water level phase prevents the invasion of marginal vegetation into the zone of fluctuation. Seeds of the annual plants that grow in that zone will not germinate until they are dewatered and woody species remain dormant until the buds are exposed to the air. Thus the constant water level phase reduces the amount of subsequent vegetation. It has also been found to be highly beneficial to fish.

The third phase is that of weekly cyclical fluctuations from the beginning of moderate *A. quadrimaculatus* production in the latter half of May till the beginning of heavy production of the species about July 1st. Thus cyclical fluctuation should have an amplitude of about one foot. The withdrawing of water from the marginal band of vegetation once a week eliminates the intersection line (see ROZEBOOM & HESS above) and provides a clean shoreline.

The fourth phase is the combination of a seasonal recession of approximately one-tenth of a foot a week with the regular weekly cycle of fluctuation.

The need for specially controlled water levels for malaria control on the main river reservoir ends about October 1st, the end of the *A. quadrimaculatus* breeding season.

In the Authority's reservoirs other than main river reservoirs, water level management is by seasonal recession alone or by cyclical fluctuation alone.

These impounded waters on the whole present less difficult mosquito control problems than do the main river reservoirs.

Norman White

KRUSE C. W. HESS A. D. & METCALF R. L. Airplane Dusting for the Control of *Anopheles quadrimaculatus* on Impounded Waters. *J Nat Malaria Soc.* Tallahassee Fla. 1944 Sept. v 3 No. 3 197-209 4 pls.

The Tennessee Valley Authority is making increasing use of airplane dusting with Paris green for the control of *A. quadrimaculatus* breeding in its impounded waters. Next season five dusting airplanes will be in operation. In this paper the authors describe the improvements that have been effected in the technique since the last report on the subject was published. A detailed description is given of the airplane, the dust hopper agitators release valve and other special equipment. Methods of calibrating the rates of discharge are described.

The dusting flying height is usually 20 to 30 feet the operation is carried out during the calm period of early morning. About 20 per cent. of the Paris green falls within the central 100 feet of the dusting swath, and 8 per cent. in the second 100 feet. The remainder drifts away and is lost. The torque of the airplane propeller causes the dust distribution curve to be skewed to the left.

A suggested revision of the specifications for Paris green for use in airplane dusting is: At least 85 per cent. shall pass a 200 mesh screen and at least 85 per cent. shall pass a 325 mesh screen at least 75 per cent. shall consist of particles 20 microns or greater in diameter (all percentages are by weight). The finer the particles the more toxic is Paris green to *Anopheles* larvae but when applied by airplane a slight breeze will cause the particles to drift away if they be too fine.

Norman White.

BISHOP E. L. & GARTRELL F. E. Permanent Works for the Control of Anopheline on Impounded Waters. (A Preliminary Report with particular reference to the Kentucky Reservoir of the Tennessee Valley Authority) *J Nat Malaria Soc.* Tallahassee, Fla. 1944 Sept. v 3 No. 3 211-19 2 figs.

The Kentucky reservoir which was scheduled for impounding in 1944 is the last and by far the largest main river reservoir of the Tennessee Valley Authority's grandiose project. It will be 184 river miles in length with an average breadth of at least 2 miles. In the central part of the reservoir water might inundate the broad flat alluvial floodplain to a shallow depth this would produce favourable conditions for *A. quadrimaculatus*. Experience gained in connexion with the Wheeler reservoir where the usual larval control measures have proved costly and incompletely effective indicated the desirability of incorporating permanent works for anopheline control in the overall construction plans for the Kentucky reservoir. This has been done. The scheme is outlined in this interesting paper. It includes diking and dewatering deepening and filling restriction of land use to daytime occupancy marginal drainage and house mosquito-proofing in a few areas. All this work is in progress or completed. By the coordination of malaria control plans with the overall plan for the reservoir it has been possible to effect savings in the capital investment essential for permanent shoreline improvement. For example a substantial economy was effected in highway and railroad relocation fills lower cost construction was possible behind the embankment built to restrict mosquito breeding areas. The complete larvicidal and shoreline maintenance programme that would have been necessary had not these permanent works been undertaken would have cost twice as much as the estimated cost of upkeep of the completed scheme. Moreover the permanent shoreline improvement scheme will provide much more effective mosquito control.

Norman White

RECTOR N H Selection of Anti-Mosquito Methods to fit Specific Malaria Control Programs. *J Nat Malaria Soc* Tallahassee Fla 1944 Sept v 3 No 3 221-6

This is a summary description of the various malaria control methods and an insistence on the necessity of making a comprehensive malaria survey before embarking on a malaria control programme

Norman White

BARRETO M P *Malária experimental algumas de suas contribuições para o conhecimento da infecção malárica no homem* [Contribution made by Experimental Malaria to Knowledge of Human Malaria Infection] *Arquivos de Hig e Saúde Pública* São Paulo 1944 May v 9 No 21 4-49 1 fig [Bibliography]

The author has successfully undertaken the formidable task of summarizing the important contributions that have been made by malarial therapy to our knowledge of human malaria and the observations on animal malaria that are concerned with the exo-erythrocytic cycle of development of the malaria parasite. The bibliography contains more than 240 references most if not all of which have been duly summarized in the pages of this Bulletin

Norman White

: TUAN CHEN The Nuclei in Avian Malaria Parasites I The Structure of Nuclei in *Plasmodium elongatum* with some Considerations on Technique. *Amer J Hyg* 1944 July v 40 No 1 26-34 33 coloured figs on 2 pls

The author has studied the structure of the nuclei in various stages of development of *Plasmodium elongatum* in canaries and ducks. Films of the blood were fixed in Flemming's fluid modified in such a manner that swelling and destruction of the blood cells was avoided. Staining was carried out by Feulgen's method and light green was used as a counter stain. There resulted a sharp contrast between the crimson nuclei and the green cytoplasm of the cell and parasite. The resting nuclei were fairly uniform in character appearing as rings which should probably be interpreted as spheres. In the dividing nuclei of schizonts purple bands appeared and it is thought that these may represent chromosomes. The nuclei of the gametocytes were less distinctive. The findings which are the same in the two hosts are illustrated in two coloured plates C M Wenyon

BLACKWATER FEVER

SHIRCORE J O A Case of Blackwater Fever in an African Girl. *Trans Roy Soc Trop Med & Hyg* 1944 Nov v 39 No 2 161-2

An African girl, born in Dar-es-Salaam had a first attack of blackwater fever when 7 years old a second attack at 9 years and a third attack reported in this paper at the age of twelve years. The present attack began on May 23rd 1944 and the patient walked to hospital next morning. When first seen by the author her temperature was 104°F but she complained only of headache and slight pain in the loins which lasted for a few days. The urine was porter-coloured for four days then became a light portwine colour until June 1st. Her blood showed a few coarse rings which were diagnosed as *Plasmodium malariae*. She was treated by Harsey's method [sodium bicarbonate and perchloride of mercury] and received also 1.875 gm. of mepacrine including an intramuscular injection of 0.375 gm. during four days. The temperature fell to

to 99.4°F on the 4th day rose to 102°F on the 7th and 8th days then fell by lysis to normal on the 12th day. She was discharged well on June 24th.

The urinary deposit was stained and examined for bacteria and a heavy infection was found, the predominant organism being a streptococcus in chains of 25 to 30 cocci. This was treated with sulphapyridine, 0.5 gm. t.i.d. on May 28th and 29th with no apparent effect on the streptococci then sulphathiazole was substituted on June 1st and within three hours the blackwater cleared and gradually became normal and free from streptococci.

The author regrets that he never examined the stained urinary deposit for bacteria in any of the 102 cases of blackwater fever which he has treated. He thinks that infection of the renal pelvis with haemolytic streptococci may be the cause of blackwater fever or at least be a contributory factor. (G. R. Ross (Researches on Blackwater Fever in Southern Rhodesia, Vol. 6 of the *Memor Series of the London School of Tropical Medicine* 1939 196 this *Bulletin* 1932, v 29 599) found streptococci in the majority of the urines examined but regarded their significance as doubtful since they are also found in non catheter specimens in other conditions with considerable frequency. HOLM (this *Bulletin* 1942, v 39 670) reported a dramatic recovery after treatment with sulphanilamide of an apparently moribund blackwater fever patient.)

J. F. Corson.

TRYPANOSOMIASIS

JACKSON C. H. \ The Analysis of a Tsetse-Fly Population. II. *Ann. Entomol.* 1944 Oct., v 12, Pl. 3 178-205 6 figs. [13 refs.]

This paper continues the treatment of data from the marking and recapture of tsetse-flies (*Glossina morsitans*) at Kakoma, Tanganyika Territory from 1935 to 1940 when the work was stopped [see this *Bulletin* 1941 v 38, 307]. All the recapture data are published, together with meteorological observations for nearly six years.

- Earlier conclusions on dispersal are confirmed—that dispersal is largely a coming and going within limits governed by vegetational boundaries and that because of this and of random returning, the average effective distance travelled by a fly in its whole life is probably under half a mile in any one direction. It is also pointed out that, for individual flies recaptured more than once the distance covered tends to be greater between the two last recaptures than between the early captures. It is conjectured that flies making longer flights may do so because they have not readily found food, and that a proportion of such individuals fail to discover food in time and are not therefore recaptured again. However another explanation might be that older flies travel more freely.

As there is some suggestion that the painting shortens life, the estimated birth and death rates should be regarded as comparative only pending the conclusion of further investigations still proceeding. An improvement has been made in the mathematical treatment which depends on the fact that the proportionate loss by death and dispersal of flies from any week of marking to the first week of recapture can be considered as approximately equal to the observed proportionate fall (which occurs in the same period) in recaptures of flies from the previous week of marking made respectively one and two weeks after it.

The bi-monthly estimates of birth and death rates are always very high in hot dry weather but in three years out of six they rise also in part of the rainy

season The estimated birth rate shows some agreement with the proportion of young flies in the catch of males and the death rate agrees with the proportion of females in the catch of flies not recognizably young Further evidence is given that females live substantially longer than males

Monthly estimates of log population are moderately well correlated with observed log density-activity ($r = +0.7$) and when numerous inherent sources of error are considered there remains little doubt that density activity reflects changes in true density rather than in activity It appears that a catch of one old (not recognizably young) male fly per 10 000 yards represents a population of some $7\frac{1}{2}$ old males per square mile and perhaps twice as many females

For various reasons arising from the experimental conditions it is not believed that the changes in density observed can be regarded as normal but a marked drop in numbers from 1935 to 1936 appears to have been of wide occurrence outside the experimental area

VANDERPLANK F L. Activity of *Glossina pallidipes* and the Lunar Cycle (Diptera) *Proc Roy Entom Soc of London Ser A* 1941-42 v 16-17 61-4 1 fig

JACKSON C H N & VANDERPLANK F L. Diameters of Mammalian Erythrocytes *Proc Zool Soc of London Ser A* 1942 Sept Pts I & II 57-60

(1) We have measured the corpuscles in dried blood films of over 200 individual mammals mostly wild East African forms belonging to about 40 species

(2) There is not a great deal of variation within the species but specific measurements vary from about 3 to 9 microns

(3) Our results agree fairly well with those of Lloyd and Johnson

(4) Closely related species unless we consider the impala as a gazelle have corpuscles of about the same size [This work was done in relation to an investigation of the species of animals on which the tsetse flies feed.—EDITOR]

GRANT J ANDERSON M & THOMPSON R B. Case of African Sleeping Sickness. *Lancet* 1944 Nov 11 624-5 4 figs

This is an account of a case of trypanosomiasis which was contracted in Nigeria about September 1941 and was not correctly diagnosed until March 1944 The patient an English soldier aged 25 was admitted to a hospital in Nigeria on September 16th 1941 (soon after his arrival in the country) suffering from enteritis a week later he had a blind boil on the right ear After another week he had fever and enlargement of the cervical glands He was treated with emetine acetarsol and sulphapyridine without benefit On November 17th 1941 a gland was removed and reported to be tuberculous another biopsy of a gland was made on December 11th 1941 in another Nigerian hospital He left Nigeria for England on January 6th 1942 and was boarded out of the army in March 1942 He then resumed his work as a clerk until December 15th 1943 with three absences from duty totalling 26 days two of these were due to transient fever diagnosed as malarial relapses and one in September 1942 was due to axillary adenitis another gland biopsy being then made and inflammatory changes of an unusual character being reported In 1943 he was very listless slow to understand what was said and to recognize people his gait was peculiar and he found it difficult to ascend stairs His speech became slurred and finally a mumble The cervical glands on the left side swelled in September 1943 his mental torpor progressed and he was admitted to hospital at Gateshead Durham on February 26th 1944 as a case of encephalitis

On admission he was apathetic and drowsy and dribbled saliva the organic reflexes were normal. The left cervical the axillary and inguinal glands were enlarged, and the skin of the left cheek and jaw was puffy and showed several patches of erythema. His temperature was normal, pulse rate 112, blood pressure 125/100. The c.s.f. was clear under increased pressure and showed excess of lymphocytes (figures for cells and protein not given). Next day an attack of streptococcal follicular tonsillitis began. Paul Bunnell test W.R. and blood cultures gave negative results. By February 29th the tonsillitis was cured but a sharp attack of facial erysipelas began which was treated with streptococcal antitoxin and sulphadiazine. By March 2nd, his temperature was normal but his pulse rate remained rapid (124) and he showed no mental change. On March 7th the existence of a tropical disease was thought possible owing to his history a blood examination showed Hb 50 per cent. (Sahli) erythrocytes 3 millions leucocytes 6 000 the sternal marrow count was normal but two trypanosomes were found in the marrow film. The c.s.f. and citrated blood were centrifuged and films made no trypanosomes were found in the blood film but they were numerous in that of the c.s.f. The formal-gel test was positive.

On March 11th he was given 1 gm. of trypanamide and in three days he began to smile and to speak spontaneously. On March 15th 2 gm. were given and then 3 gm. weekly up to 30 gm. On March 18th the facial erysipelas relapsed and his mental condition deteriorated and he had incontinence of urine but the erysipelas was soon cured and his mental condition gradually improved. On March 27th he spoke freely though with some slurring the c.s.f. showed 98 cells and no trypanosomes and on May 5th it was normal except for a slight increase of protein (figures not given). He was transferred to Liverpool to the care of Dr. A. R. D. ADAMS who found the c.s.f. cell count to be 10-12 protein 0.04 per cent. globulin slightly increased and glucose normal. In July he returned to work and in September he was still well. (This case illustrates the difficulty of diagnosis in some cases of Gambian sleeping sickness a matter of special importance at the present time when many soldiers and others are returning from tropical Africa.)

J. F. CORSON

- f) HARDING R. D. & HAWKING F. Diagnosis of Sleeping Sickness. [Correspondence] *Lancet* 1944 Dec. 23 835

Referring to the paper by GRAY, ANDERSON and THOMPSON [above] the authors draw attention to two methods of diagnosis of trypanosomiasis which are more effective than blood examination. The first is gland puncture which is known to medical officers in tropical Africa and introduced by GRAY and GRAY in 1904 see *Sleeping Sickness Bulletin* 1908 v. 1 No. 2 54. Harding found that when both methods were used in infected cases the results were as follows: both positive 30-40 per cent. gland puncture positive blood film negative 50-60 per cent. blood film positive gland puncture negative 10 per cent.

The second procedure is culture of the trypanosomes by the method of BRUTSAERT and HENKARD [this *Bulletin* 1938 v. 35 704] which HAWKING [ibid., v. 37 1940 697] found to be simple and practical. Weinman's method [ibid. 1944 v. 41 653] is also mentioned but Hawking found it less satisfactory than the other as microscopical examination was more difficult. The procedure is as follows: 5 cc. of the patient's blood is prevented from clotting by mixing with 1 cc. of a 1 per cent. solution of heparin. About 0.2-0.5 cc. of the mixture is added to 2 cc. of human or guinea pig blood, containing 1 per cent. of sodium citrate in each of 10 tubes. The anticoagulants may be omitted if the infected blood is added quickly before it has time to clot. The

are capped and incubated at 24-30°C. Sterile precautions must be taken. The contents of the tubes are examined microscopically after 10 and 20 days by taking a small sample both from the surface and from the depths of the layer of red cells. The trypanosomes are actively motile but are very unevenly distributed and a prolonged search may be necessary.

BROWAEYS J. Inoculation d'un ou de plusieurs trypanosomes à la souris [Inoculation of One or of Several Trypanosomes into Mice.] *Bull Soc Path Exot* 1943 May 12 & June 9 v 36 Nos 5-6 147-50 1 fig

The author studied the infections produced in mice by the injection of different numbers of trypanosomes varying from a single trypanosome to six or more. He used a strain of *T. brucei* of the Institut Pasteur Paris which was of moderate virulence killing mice in about 9 days. The injections were made subcutaneously. The results are shown in a chart. The incubation period usually diminished as the number of trypanosomes injected was increased but the duration of the disease appeared to be unrelated to the dose of trypanosomes. A mouse which received four trypanosomes had a chronic infection lasting 30 days while two mice each infected with a single trypanosome died in four days after incubation periods of 9 and 10 days respectively. Except in one doubtful case all mice receiving more than two trypanosomes became infected with one or two trypanosomes however the results were sometimes negative but on reinjection with 3, 4 or 5 trypanosomes the mice became infected. Reference is made to earlier work by PROVAZAK [this *Bulletin* 1913 v 2 39] OEBLER [*ibid* 1913 v 1 525 v 2 359] HENNINGFELD [*ibid* 1914 v 3 429] and TOPACTO [*ibid* 1934 v 31 215].

POURAINES Y & FIGOURY L. BORDY R & BERNARD M. Trypanosomose expérimentale du cheval à *Trypanosoma evansi* (souche syrienne). I. Etude clinique [T. evansi Infection of the Horse I. Clinical Study] *Bull Soc Path Exot* 1943 July 7 v 36 Nos 7-8 235-44 4 figs. on 2 pls.

POURAINES Y & FIGOURY L. Trypanosomose expérimentale du cheval à *Trypanosoma evansi* (souche syrienne). II. Études sérologique et hématologique. [T. evansi Infection of the Horse II. Serological and Haematological Studies.] *Bull Soc Path Exot* 1943 July 7 v 36 Nos 7-8 244-56 4 figs. on 2 pls.

LWOFF Marguerite & NICOLLE P. Recherches sur la nutrition des réduvadies hémophages. II. Besoins alimentaires des adultes de *Triatoma infestans* Kling dans les conditions habituelles d'élevage. Fécondité des femelles. [Food Requirements of T. infestans. Fertility of Females.] *Bull Soc Path Exot* 1943 Mar 10 & Apr 14 v 36 Nos 3-4 110-24 2 figs.

NICOLLE P & LWOFF Marguerite. Recherches sur la nutrition des réduvadies hémophages. III. Alimentation artificielle de *Triatoma infestans* Kling au moyen de sang défibriné hémolysé. [Artificial Feeding of T. infestans with Defibrinated Haemolysed Blood.] *Bull Soc Path Exot* 1943 May 12 & June 9 v 36 Nos 5-6 154-67 8 figs.

LEISHMANIASIS

Kirk, R. Studies in Leishmaniasis in the Anglo-Egyptian Sudan. VI.—The Evolution of Leishmania Infections in Man. *Trans Roy Soc Trop Med & Hyg* 1944 Aug v 38 No 1 61-70 [24 refs.]

In discussing the evolution of leishmania infections in man the author notes that three main types of disease occur viz. oriental sore kala azar and American mucocutaneous leishmaniasis. Actually there is no hard-and-fast line of demarcation between these three types. Thus typically oriental sore is a purely cutaneous infection at single or multiple foci the termination of which is followed by complete immunity but it is becoming evident that in kala azar there is a primary skin lesion which instead of healing and leaving a solid immunity leads to a generalized infection and the disease kala azar. Again in the American mucocutaneous disease a primary purely cutaneous infection occurs and often behaves as oriental sore healing and establishing an immunity. In some cases, however following the healing of the primary sore after a varying interval the lesions in the mucosae of the nose mouth or pharynx appear. The author points out that though he has seen no record of any generalized infection following the healing of the primary sore it is inconceivable that such does not occur in those cases in which the mucosal lesions subsequently develop. This development of the mucosal infection in the American disease is analogous to the cutaneous eruptions known as dermal leishmanoid which in India and the Sudan follow recovery from kala azar.

While the three disease types mentioned above may be clearly defined, it appears that transition forms not infrequently occur. In oriental sore for instance there is evidence that sometimes infection is not limited to the skin, while symptoms suggesting a generalized infection have been noted. In kala azar leishmania have been found in the nasal mucosa and tonsil. The author has noted the appearance of lesions in the mucosae of the nose and mouth simultaneously with the development of the post-kala-azar cutaneous eruption while in India observers have described a similar ulceration of the lips palate and tongue.

In the Sudan the author has come across a number of cases in which the three main types merge into or follow one another so that there may be a difficulty in deciding whether a case is one of oriental sore or of a primary lesion of kala azar or again whether a case is one of mucocutaneous leishmaniasis or whether the mucosal lesions are the expression of a post-kala-azar condition. It is only by observations over long periods that a final decision can be made in such cases.

In discussing the reasons for the variations the author suggests that most are due to the existence of different strains of leishmania of varying virulence and tendencies. The marked difference between strains of leishmania causing oriental sore and kala azar are well recognized, but minor differences occur within these groups. The leishmania of Indian, Sudan, Mediterranean and Chinese kala azar are not identical in all respects and similar variations occur between the leishmania of oriental sore in different localities. Even in adjacent areas the same disease may show that the causative organisms are not quite alike and are undergoing evolutionary changes. Thus post-kala-azar dermal leishmaniasis is a common sequel of the disease in Bengal, but it is rarely seen in Assam where the disease is of epidemic character. Recently Russian workers have claimed that the two types of oriental sore occur in Turkestan (see this *Bulletin* 1944 v 41 332). There is evidently much to be said for the author's point of view which he has carefully and logically expounded in this very interesting paper.

C. M. Wemyss

PIFANO C F. Notas sobre entomologia médica venezolana. I. Fleboton transmisores de leishmaniasis tegumentaria en el valle del Yaracuy [Notes on Medical Entomology in Venezuela. I. *Phlebotomus* as Vectors of Dermal Leishmaniasis in the Yaracuy Valley] *Bol. Ent. Venezol.* Caracas 1943 v. 2 No 2 99-102. English summary. [Summary taken from *Rev. Applied Entom.* Ser. B 1944 Nov. v. 32 Pt. 11 216]

Investigations on dermal and mucocutaneous leishmaniasis attributed to *Leishmania brasiliensis* were made during the years 1938-40 in a part of the State of Yaracuy, Venezuela, where the infection occurs frequently in man under various forms in the rural areas and is also found in dogs. The endemic zone is very damp during the rainy season when it is subject to floods and the vegetation is luxuriant. Adults of *Phlebotomus longipalpis* Lutz & Neiva, *P. migonei* Franca, *P. intermedius* Lutz & Neiva and *P. davisi* Root were taken in dwellings feeding on persons with leishmanian lesions and *P. migonei* was also taken on dog. *P. maracayensis* N. Toy was found in a fowl house. Descriptions are given of flagellates found in *P. migonei*, *P. longipalpis* and *P. davisi* and morphologically identical with the culture forms of *L. brasiliensis* from mucocutaneous lesions.

GUPTA J C & KAHALI B S. General Pharmacology of Umbellatine, a New Alkaloid Isolated from *Berberis umbellata* Wall. and *Berberis insignis* Hook. *P. and its Use in the Treatment of Oriental Sore* *Indian J. Med. Res.* 1944 May v. 32 No 1 53-6 [12 refs.]

In a pharmacological study of umbellatine, an alkaloid ($C_{22}H_{25}O_3N$) isolated from *Berberis umbellata* and *B. insignis*, it was found to be similar to berberine but more intense in its action except in the cardio-vascular responses which were feeble than those produced by berberine. As berberine acid sulphate in 2 per cent solution (orisol) has been employed with some success for the infiltration treatment of oriental sore, the authors tested the new alkaloid in 0.5 per cent solution in the treatment of a number of cases. Small uninfected sores were cured by one or two injections but sores with secondary infections required from 10 to 12 weekly injections. In one case with two infected sores one was treated with the new alkaloid and the other with orisol. The two sores healed simultaneously. The authors consider the results obtained to be encouraging. It is claimed that umbellatine in a strength of 1:50,000 inhibits the growth of *Leishmania tropica* in a liquid haemoglobin saline medium whereas at five times the strength it has no action on *L. donovani*.

C. M. Wenyon

FEVERS OF THE TYPHUS GROUP

GROMASHEVSKY L V & STEPANOV I R. [Observations on the Epidemiology of Exanthematic Typhus.] *Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii* Moscow 1944 No 3 52-6 [In Russian]

Of 488 outbreaks of typhus 40 per cent occurring in rural districts consisted of single cases only. These single cases did not differ in clinical picture or any other respect from those which led to multiple outbreaks. The latter soon died out in all cases in spite of the fact that hospitalization was delayed on an average to the 5th-8th day of the disease and in some cases as late as the 12th day. The early suppression of the disease in spite of the delay in hospitalization

was attributed to the low incidence of lousiness in the population—five cases were actually not admitted to hospital, yet did not give rise to any secondary cases. The authors nevertheless consider that a further reduction in the incidence of the disease could be obtained if earlier hospitalization and more vigorous countermeasures were practised.

D J Baxter

CORRIGAN S S & CRABGAFF E. Studies on the Composition of *Rickettsia prowazekii*. *J Biol Chem* 1944 Aug v 154 No. 3 691-704 3 figs [16 refs]

The studies described in this paper were of a highly technical kind—they were carried out at the request of Colonel H. PLOTS who supplied the necessary formalized yolk-sac cultures of *Rickettsia prowazekii*.

By various procedures involving the use of the ultracentrifuge and electrophoresis it was possible to isolate specific antigenic substances and to determine some of their chemical, immunological and protective properties. They were found to consist of high-molecular carbohydrate-protein complexes—nucleic acid and lipid fractions were also isolated.

The original paper must be consulted by those who are interested in this kind of investigation which can be carried out only by highly specialized workers who have the necessary laboratory equipment at their disposal.

John W D Negro

ANDERSON C. R. Experimental Typhus Infection in the Eastern Cotton Rat (*Sigmodon hispidus hispidus*). *J Exper Med* 1944 Nov 1 v 80 No. 5 341-56. [11 refs]

This paper is rich in technical information which will be highly valued by those who are working on the fundamental problems of the fevers of the typhus group. Of general interest is the discovery that cotton rats are highly susceptible to classical and murine strains of typhus rickettsiae. By using large doses of the infecting material it was found possible to produce fatal infections by both types of the organisms.

So far as the author knows there is only one other animal—the South-African gerbil—which shares this degree of susceptibility to the two infections.

Transmission of uniformly fatal infections through an unlimited number of passages was achieved by the intracardial or intracerebral injection of large doses of suspensions made from the livers of infected cotton rats. An important point was the removal of the liver at the time of maximum infectivity. Larger doses were needed in the case of murine than of epidemic infection. Although the lethal dose was large the immunizing dose was relatively small—the lethal dose was about 10 000 to 100 000 times larger than the immunizing.

Rickettsiae were easily demonstrated in smears made from the liver or brain, also from exudates into the peritoneum and pericardium.

A partial degree of cross immunity was demonstrated between the murine and epidemic types of infection. Sera of the infected animals did not agglutinate *Proteus OX19*. Very little trouble was experienced from secondary infections among the animals. Three strains of classical rickettsiae and two of murine were tested and though these came from widely separated parts of the world all of them were capable of causing uniformly lethal infection in the animals.

The author thinks it possible that a strain of rickettsia may be found which will be neutralized in high titre by sera of both epidemic and murine origin. Some of the strains already investigated appear to cross more than others when used as antigen in the neutralization test.

It is mentioned that the data obtained by the U.S.A. Typhus Commission show that the complement fixation test is an accurate means of diagnosis.

[From the context it appears that this statement applies to the differential diagnosis of classical from murine typhus] *John W D Megaw*

RUIZ CASTAÑEDA M & ROBERTO SILVO G Preservation of Classic *Rickettsia prowazeki* in the Lungs of Mice after 74 Consecutive Transfers. *J Infect Dis* 1944 Sept.-Oct v 75 No 2 103-5

The special point in the technique adopted by the authors was the addition of sterile sulphathiazole to the suspensions of mouse lung used in making the transfers of infection from lung to lung. By this means secondary infections were kept in check, and it was found possible to make 74 successive transfers of two strains of *Rickettsia prowazeki* through the lungs of mice by intranasal inoculation.

The original inoculum consisted of tissue cultures of fragments of tunica vaginalis which were removed from infected guineapigs on the 8th or 9th day after inoculation. After one or two lung transfers virulent pulmonary infection was established, and the addition of sulphathiazole to the lung suspensions used in making the transfers prevented complicating infections by Gram positive cocci.

In spite of this precaution two kinds of secondary infection sometimes occurred. One of these was a bacteria free pneumonia caused by virus infection; this was frequent, and in some of the affected mice it was observed that the usual bacilli form rickettsiae were replaced by considerable numbers of very small cocci whose nature has not yet been investigated. The other secondary infection was by Gram-negative organisms whose presence did not prevent the development of the rickettsiae, but when the organisms were inoculated intraperitoneally into guineapigs they caused a fatal infection accompanied by scrotal swelling. Rickettsial strains obtained from tunica washings of guineapigs infected with these organisms did not cause orchitic lesions, but did cause typical classical infection.

The maintenance of the classical strains of rickettsiae for an indefinite number of passages were found to be of great help in the routine preparation of the bivalent vaccine employed by the senior author. *John W D Megaw*

LEON A. P. El concepto unicista de la etiología del tifo exantemático y la clasificación de la *Rickettsia prowazeki*. [The Unitary View of the Aetiology of Typhus Exanthematicus, and the Classification of *Rickettsia prowazeki*] *Rev Inst Salubridad y Enfermedades Trop* Mexico 1944 June v 5 No 2 137-52 1 folding fig [30 refs] English summary

The author produces further evidence to show that there is no uniform association either between murine or endemic typhus and orchitic strains of rickettsiae or between human or epidemic typhus and non-orchitic strains. He prefers the name vaginalitic as a designation for strains in which pronounced scrotal reactions occur regularly in successive passages through guineapigs and non vaginalitic for strains which cause either no such reaction or one that is late and transitory. The disease in man is regarded as epidemic when the evidence points to transmission from man to man, and as sporadic when there is no evidence of such transmission.

Among 36 cases investigated by the author 29 strains were isolated of which three were definitely vaginalitic and one was doubtfully so. One case was of special interest: a married couple were attacked by typhus fever three days after arrival from a place where the disease was prevalent in epidemic form. 16 days later one of their children was attacked and within the next six days 7 others were attacked. Twenty days after the onset of the last of these cases a

woman who had washed the clothes of the family was attacked, and from her blood a definitely vaginalitic strain was isolated. The family, and their clothing were heavily infested with lice and obviously the infection had been transmitted at least three times through the cycle man-lice-man. In another case of vaginalitic infection the evidence of louse transmission was equally clear.

Of the patients from whom non vaginalitic strains were isolated 19 were louse-infested and were attacked during an epidemic—only one was a sporadic case in a louse-free person.

Great variations were found in the virulence of four non-vaginalitic strains as judged by their lethality to rabbits—one killed 61.4 per cent. of the rabbits that were inoculated, another killed only 12.5 per cent. The only vaginalitic strain studied in this way killed 18.3 per cent. of the inoculated rabbits and the original Mooser vaginalitic strain did not kill any of 15 rabbits inoculated with tunica vaginalis material.

The author quotes the observation of ZWIERZ [this *Bulletin* 1938 v 35 786] who isolated a strain from rats and passaged it 13 times through guinea-pigs none of which showed an orchitic reaction. The conclusion reached is that typhus exanthematicus is caused by a single species of rickettsia of which there are two strains *R. prowazeki prowazeki* and *R. prowazeki mooseri*—the former is non-vaginalitic and the latter vaginalitic. Either strain can cause epidemic or epidemic typhus and either can be of high or low virulence according to the conditions in which transmission occurs.

[It is becoming clear that if there are two species of rickettsiae—one of which causes flea-borne typhus and the other louse-borne typhus, they cannot be differentiated with certainty by the presence or absence of orchitic properties but it does not follow that there are no specific antigenetic differences between them. Recent work on complement-fixation and rickettsia agglutination reactions suggests the possibility that such differences may exist though much more work will be needed before a final verdict can be given on this question.]

Taking the broad view it is usually easy to decide whether transmission is from man to man by lice or from rat to man by fleas—but in conditions in which both of these modes of transmission are epidemiologically possible physicians and public health workers cannot yet rely on the results of animal experiments as safe guides to the measures of prevention that are needed. In such cases the only safe rule is to control both lice and rats.] *John W. D. Megaw*

VAN ROOYEN C. E. with the technical assistance of D. DARSIN, G. R. POLLACK & W. G. C. BEARCKOFF. Typhus Rickettsial Agglutination Tests in the M.E.F. and Egypt. *J. Egyptian Pub Health* 41: 1944 June v 19 No. 6 23-68, 3 charts.

The author has already described the results of rickettsia-agglutination tests carried out in 50 cases of typhus-group fevers in the Middle East [this *Bulletin* 1943 v 40 885]. The continuation and expansion of the previous investigation are dealt with in the present paper and the former conclusions are regarded as having been confirmed. In 523 cases the agglutination titres of "epidemic" and murine strains of rickettsiae have been tested (these reactions will be referred to as E.R. and M.R.)—in many cases the Weil-Felix test was also carried out. *Proctus OX19*, *Pr OX2* and *Pr OAK* were employed (these reactions will be called *OX19 OXS* and *OXK* respectively).

A study of the typhus fever prevailing among Egyptians showed that the disease was of the epidemic type though from the data supplied in the paper a few of the cases seem to have given ambiguous responses—for example in one case tested on the 7th day the E.R. and M.R. titres were each 200 and guinea-pig inoculation gave a negative result.

In Palestine the disease is known to be chiefly murine in type the official reports show that in 1942 there were 275 cases with only 2 deaths and that the chief season of prevalence was in the months August to November Correspondingly the reactions of military patients stationed in Palestine were of the M R type in the great majority of cases

Sera from 81 civilian patients in Iraq and Iran were tested in the months of February March and April 1943 the reactions of 75 were of the E R. type and only 6 M R reactions were observed These results were in agreement with those observed in military patients from the area

Clinical and laboratory details are given of each of the 50 cases whose reactions were reported in the previous paper but information regarding the epidemiological conditions is seldom sufficient to justify an opinion as to which vector was concerned in transmission in a particular case When the E R was positive at a higher titre than the M.R. the case was regarded as being of the epidemic louse borne type and when the M.R. titre was higher the diagnosis was murine typhus [It should be pointed out that in 9 of the cases diagnosed as murine the M R titre ranged from 300-2 000 was only twice or less than twice as high as the E.R. titre which ranged from 200-1 600 and in 4 of the cases diagnosed as epidemic the E.R. titre ranged from 800-2 000 and the M R titre was half as high in each case. In the later tests there were fewer cases in which the difference between the titres was so small but the occurrence among 323 patients of nearly 40 cases in which the titre was only twice as high for one strain as for the other suggests that the test cannot always be relied on for the differentiating between the two strains.]

The author discusses the occurrence of cases in which the O12 titre was exceptionally high the following examples are of interest in this regard —

Locality of occurrence	OX19	OX2	OXA	E R.	M R	Diagnosis
Sarafand	400	5 000	400	200	300	Murine typhus
Gaza	100	3 200	200	0	50	Do
Cairo	200	1 600	400	0	0	O12 type

The case from Sarafand is said to have been vaguely suggestive of tick typhus but later it is stated that there has been no evidence to hunt that our cases were associated with the bites of ticks [The Sarafand patient is said to have crushed ticks from his dog and the clinical description seems to be more in keeping with the diagnosis of tick typhus than of flea typhus. These and some other cases suggest that the possible occurrence of tick typhus in the area ought to be considered. It would be surprising if the tick borne disease were absent from the area.]

Many guinea pig inoculations were carried out and 28 epidemic strains were isolated from patients and their lice Attempts were made to isolate strains from six cases of clinically typical mild murine typhus in Egypt but only one guinea pig reacted and even in this the strain died out on secondary passage. Positive M.R. reactions (1-40 to 1-800) were observed in more than half of 38 wild rats *Rattus norvegicus* trapped at three desert camps where 24 cases of mild murine typhus had occurred all the rats gave negative responses with the E R test. The number of positive reactions among other groups of rats is shown in the table below. Reactions of 1-100 and over were counted as positive. It is claimed that R.A. tests should prove invaluable in elucidating the precise nature of all suspected cases of typhus fever and that it would contribute towards the better description of typhus fever if the terms epidemic and endemic were discarded and instead the disease were labelled

Place of Origin	Number of rats	OVI9	MLR	E.R.
Laboratory white rats	56	18	0	0
Palestine (various localities)	514	44	88	13
Port Said Docks	74	3	24	0
Cairo	120	9	1	0

according to the insect vector responsible e.g. louse, flea tick and mite-borne typhus. The introduction of the R.A. test brings such a classification within the bounds of reality."

[The comments made on the previous paper written by the same author hold good for the present article. He has produced important evidence in favour of the hypothesis that louse-borne and flea-borne typhus can be differentiated by serological tests but the reviewer is reluctantly compelled to regard the argument as being not yet proved.]

John W. D. Meegan

SMORODINTSEV, A. A. & DROBYSHEVSKAYA, A. I. Early Diagnosis of Typhus Fever through Detection of a Specific Antigen in the Blood. *Amer. Rev. Serid. Med.* 1944 Feb v 1 No 3 229-32.

SMORODINTSEV and FRADKINA have already described a rapid slide-agglutination reaction for detecting the presence of a specific antigen in typhus fever at an early stage of the illness while antibody formation has not yet progressed so far as to neutralize the antigen. [See this *Bulletin* 1944 v 41 1021]

In the present paper the authors describe a complement-fixation reaction by which the same result is said to be obtained.

The reaction is strongest during the first few days of the attack and becomes progressively weaker as the production of antibodies increases so that by the 10th day it ceases to be positive. Correspondingly the Weil-Felix reaction, which depends on the presence of antibodies, is negative at first and becomes progressively stronger.

Results obtained by the test, and by the Weil-Felix reaction in the same patients are shown in the table. The figures in brackets show the number of cases in which the reaction was positive for the particular test and negative for the other.

Days of the fever	Number of patients tested	Positive Complement fixation	Positive Weil-Felix
1-2	13	13	0
3-4	18	11	0
5-6	78	44 (31)	29 (16)
7-8	75	33 (17)	43 (29)
9-10	32	12 (?)	21 (11)
Over 10	38	0	33

The controls consisted of 57 patients suffering from typhoid, dysentery, pneumonia, etc. all gave negative reactions with both tests. The technical details cannot be summarized. Sera for test were inactivated at 56°C. for 3 minutes and were used in 1:3 dilutions. The antisera were obtained from typhus convalescents after the 7th afebrile day—these were inactivated in the same way and were diluted 1:10. In each test 0.2 cc. of diluted patient serum and of antiserum were mixed in each of four tubes to which were added

varying quantities of titrated complement. The tubes were kept at 0-2°C for 18 hours. Sensitized erythrocytes were added and the tubes were kept at 37°C. Readings were made as soon as haemolysis occurred in the three sets of control tubes which were used in each batch of tests.

The authors expect that the sensitiveness of the reaction will be increased by using anti rickettsial serum obtained from hyperimmunized rabbits instead of human convalescent serum as the antiserum.

John W. D. Megaw

FROMME W & GAASE A. Zur Spezifität der Proteus OX19-Agglutination nach Weil-Felix. [The Specificity of the Weil-Felix Reaction for Proteus OX19] *Munch med Woch* 1943 July 16 v. 90 No 28/29 415-16

Careful Weil-Felix tests were carried out in 8 600 presumably healthy persons whose sera were being tested to exclude syphilis. Readings were made after the tubes had been kept two hours in the incubator and again after a further period of about 20 hours at room temperature. It was found that more than one-quarter of the cases with end titres of 1-100 or over would have been returned as negative if the first reading only had been made. In a few of these cases the 24 hour titres were quite high.

Among the 8 600 sera 445 gave positive reactions. The titre was 1-100 in about half of the cases and 1-200 in 44 per cent. In two it was 1-3,200. An attempt was made to investigate the association between positive reactions and previous exposure to the risk of typhus infection and it was found that in 41 per cent. of the reacting persons there had been some contact with typhus conditions or there had been antityphus inoculation. The author concludes that the reaction was likely to have been specific in these persons so that the percentage of presumably non-specific reactions would be reduced from 5.2 to 3.1 and he believes that even the latter figure is too high because there might have been an unknown association with typhus conditions in many cases in which the persons gave negative histories. In support of this view he mentions the curious fact that the proportion of positive reactions was nearly twice as high in June as in April. This increase in the number of positives is attributed to the occurrence of inapparent attacks of the disease during the typhus season. He also found that there was a close degree of correspondence between the types of reaction occurring in the person with and in those without a history of association with typhus conditions. In both groups about 50 per cent. of the reactions were at a titre of 1-100. [Titres of 1-400 and higher were however three times more numerous among those with a history of contact with typhus conditions than among those with no such history.] The author further argues that if the reactions are not regarded as positive unless the titre is at least 1-200 the non-specific reactions would be reduced to the remarkably low percentage of 1.2. The only clear evidence of non-specific reactions was found in connexion with jaundiced persons. 8 per cent. of these gave positive reactions. The author concludes that the reaction reaches a high standard of specificity as a test for typhus fever.

John W. D. Megaw

BRUMPT L. L'hémoagglutination rapide appliquée au dépistage du typhus exanthématique. [The Application of a Rapid Blood-Agglutination Test for detecting the Occurrence of Typhus Fever] *Bull Soc Path Exot* 1943 May 12 & June 9 v. 36 Nos 5-6 175-87 1 fig & 1 pl. (chart & coloured figs)

The author with enthusiasm that appears to be justified describes the practical application of the simple agglutination test devised by himself in 1940.

He calls the test the haemodagnostic or H D test. It has been applied by him in thousands of cases not only for the detection of typhus fever but also—with appropriate bacterial suspensions—for brucellosis, fevers of the enteric group and bacillary dysentery.

In typhus fever he has the impression that the test is even more reliable than the standard Weil-Felix reaction. The technique, in outline, is as follows. A 24 hour agar culture of *Proteus OX19* is mixed with a 10 per cent. solution of citrate of soda to make a milky suspension, which is titrated so as to give a reading of 100 with the Vernes photometer after being diluted 1-20. Commercial formal is added to make a strength of 0.5 per cent. One drop of 1-0 per cent solution of pure methylene blue is added to each cc. of the suspension. After keeping at room temperature for a few days the suspension is filtered through cotton wool. It keeps well for at least six months preferably in sealed ampoules kept in the ice box.

A drop of the suspension after shaking is placed on a slide half as large as drop of finger blood is picked up on the corner of a glass slide and stirred into the suspension so as to make a pool of 15 mm. diameter. The pool should then be brownish green in colour if it is pure green the quantity of blood is not enough. The slide is placed on a white porcelain plate which is rocked with the movement used in rolling a marble round a plate. This movement is an essential part of the technique. In negative reactions no change is seen in the specimen these may occur when the Weil-Felix titre is less than 1:100. When a thin discontinuous narrow blue ring appears within 4 minutes the reaction is considered to be doubtfully positive. A continuous narrow blue ring at the margin of the drop appearing within two minutes, corresponds roughly to a Weil-Felix titre of 1-200 to 1-800. A thicker blue ring in which fine granules are seen within one minute corresponds to a titre of 1-400 to 1-1,600. A broad deeply stained ring appearing in 30 seconds corresponds to 1-800 to 1-3,200. When large blue granules appear at once and encroach on the central part of the pool a still higher titre is indicated.

The author points out that the Weil-Felix titre is far from having an accurate mathematical significance. Different observers employing different strains and different techniques will obtain widely varying results with the same sample of serum.

If the H.D. test is carried out on a piece of fresh photographic paper with a smooth gelatin surface a permanent record of the result can be obtained. The paper is first fixed with hypo then washed and dried. When the reaction is complete, and in any case within four minutes the liquid is pipetted off and the paper is allowed to dry in the air for fifteen minutes or so. It is then washed in water to remove the remaining red blood cells so that only the blue ring is left. A coloured plate shows the different types of reaction that occur.

The method is now widely used in French North Africa by physicians and medical officers of health. With proper organization as many as a hundred tests can be carried out within an hour.

John W. D. McGarr

BISCHOFF G. Ueber Ergebnisse mit einer Hautprobe bei Fleckfieber. (The Results obtained by a Skin Test in Typhus Fever.) *Klin. Woch.* 1943 Mar 13 v. 22 No. 11 227-30.

The test consisted in the intracutaneous injection of 0.15 cc. of the weakest strength of Weigl's louse vaccine. Reactions were regarded as positive when a zone of redness of at least 1.0 cm. diameter persisted at the end of two days. A red linear streak or a lentil-sized zone of redness was regarded as negative. Healthy persons and patients suffering from diseases other than typhus gave positive reactions provided that they had neither suffered from typhus

fever nor been vaccinated with Weigl's vaccine. Typhus patients as well as healthy persons who had previously been inoculated with Weigl's vaccine also gave positive reactions.

About three-fourths of the typhus patients who had not been vaccinated gave negative reactions when tested between the 6th day of the fever and the 15th day after the end of the fever. These negative reactions were regarded as indicating the presence of specific neutralizing antibodies.

The positive reactions in typhus patients who had been vaccinated were regarded as being due to anaphylaxis associated with the albuminous substances contained in the louse vaccine.

John W. D. Megaw

GIROUD P. Réactions d'hypersensibilité cutanée à l'antigène tué test clinique de l'immunité chez les anciens typhiques et les sujets vaccinés. [Reactions of Cutaneous Hypersensitivity to Killed Antigen, a Clinical Test of Immunity in Previous Cases of Typhus Fever and in Vaccinated Persons.] *Bull. Soc. Path. Exot.* 1943 May 12 & June 9 v. 36 Nos. 5-6 134-45.

The author gives an account of the practical applications of the skin sensitivity test devised by himself. The antigen used in the research was prepared from the lungs of infected mice or rabbits. Egg yolk cultures and suspensions made from the intestines of lice were not suitable because they were found to give rise to false positives in some normal persons.

A positive reaction is regarded as clear evidence of a previous attack of typhus fever: it occurs after mild or inapparent as well as after severe attacks. In very debilitated persons the reaction was sometimes negative even after the occurrence of proved attacks.

The author believes that persons who give frankly positive reactions are in a state of premunition and therefore need not be vaccinated. When vaccinated persons show slight and incomplete reactions they are regarded as being partially protected: a pronounced reaction indicated immunity.

The author believes that many persons who have been exposed to infection after having been vaccinated suffer from inapparent infection which greatly increases their immunity. Even after attacks of the disease there may be a disappearance of the active immunity as is shown by the occurrence of negative skin reactions. All persons who fail to show positive reactions need vaccination or revaccination.

Two different strains of antigen were used: one of North African and one of Eastern (de l'Est) origin; both of these gave very similar response when used in testing former cases, whether of North African or Eastern origin.

John W. D. Megaw

WOODWARD T. E. in collaboration with E. F. BLAND. Clinical Observations in Typhus Fever with special reference to the Cardiovascular System. *J. Amer. Med. Ass.* 1944 Sept. 30 v. 126 No. 5 287-93 3 figs. [Refs. in footnotes.]

The authors describe and discuss the cardio-vascular disturbances observed in 30 patients who were closely studied in a hospital in French Morocco. The investigation formed part of the work of the U.S.A. Typhus Commission.

It was concluded that the abnormalities of the circulatory system were due chiefly to the foci of necrosis in the smaller vessels. The resultant lack of blood vessel tone and reduction in circulatory blood volume were regarded as far more important factors than cardiac insufficiency. Electrocardiograms made in the most active stages of the illness, sometimes even when the patients were on the point of death, showed no striking evidence of high-grade conduction defects or of important changes in the T wave: minor abnormalities were

observed in rather less than half of the cases. The venous pressure was consistently low 2-12 cm. water. It was not increased by intravenous injections of 1 000 cc. of fluid, so that there did not appear to be any important element of cardiac weakness. X ray photographs taken in 12 cases, showed no evidence of cardiac enlargement.

When dehydration had been overcome the red cell count was found to be 2,500 000-3 700 000 per cmm. and the volume of cells was reduced to 23-42 volumes per cent. There was a tendency to leucopenia the usual white cell counts were 4 000-6,000 per cmm. higher counts up to 10 000 per cmm. were found in association with pyrogenic infections. The total protein content of the blood serum averaged 5.2 gm. per 100 cc. the albumin element was often very deficient and sometimes was as low as 0.6 gm. per 100 cc. while the globulin element showed a lesser reduction. Blood chlorides were reduced, and associated with this finding there was alkalosis in semiconscious patients.

There was little evidence of renal damage the urine was often free from albumin, but oliguria was often pronounced in the early stages in spite of a fluid intake of 4 000-5 000 cc. Non-protein nitrogen was high in severely ill patients who had not received supportive treatment but this azotaemic condition could be corrected by giving chlorides and overcoming dehydration, so that it did not appear to be due to renal damage. Only two of the 30 patients died, and one of the deaths was in the case of a woman aged 73 who was admitted late in the second week of the illness. The treatment was on supportive lines, the points specially emphasized being: (1) careful nursing with frequent changes in position, (2) A daily fluid intake of at least 4 000 cc.—when possible by the mouth but if necessary partly by intravenous injection. (3) A few patients were given transfusions of dried blood plasma with excellent effects. (4) 2-4 gm. doses of ammonium chloride improved the hypochloraemia. (5) An indwelling stomach tube was found useful when the patients could not be induced to swallow enough supporting foods. (6) digitals and other cardiac stimulants were not indicated in any of the cases, though in congestive heart failure or auricular fibrillation they would be likely to be of value. (7) sulphonamides were given in small doses for purulent infection no ill effects were observed.

[This paper deserves special attention because of clear evidence produced by the authors that the maintenance of nutrition and the prevention of dehydration are factors of primary importance in the treatment of typhus fever. Several German observers have recently pointed out that circulatory failure in this disease is commonly caused not by cardiac damage but by disturbances of the vasomotor centres due to intoxication and interference with their blood supply the latter resulting from lesions of the smaller blood vessels.]

John W. D. Megaw

SCHÖLLER, H. Krankheitserscheinungen des Nervensystems bei Fleckfieber [Signs and Symptoms of Nervous-System Origin in Typhus Fever] *Klin Woch* 1943 Apr 3 v 22 No 14/15 299-305. [31 refs.]

In a long and rather discursive paper the author deals with the signs and symptoms of typhus fever which are associated with damage to the nervous system. An attempt is made to correlate each manifestation of the disease with a particular lesion or group of lesions in the central or peripheral nervous structures. The author himself has not undertaken the difficult task of supplying a summary of the article for reasons that will be obvious to those who read its contents.

The great variability of the nervous disturbances is stressed this point is emphasized by the length, but of those that are discussed

A few of them are as follows—Features of the early stages of the illness are headache signs of meningeal irritation supersensitiveness to external stimuli

apathy trismus partial deafness and somnolence. In the later stages from the end of the first week onwards there may be auditory or visual hallucinations delirium loss of orientation to time and place motor unrest dual personality epileptiform convulsions hemiplegic seizures stupor amentia acute catatonia confusion incoherence of speech and thought insomnia mutism tremors choreiform movements tetany difficulty in protruding the tongue muscular incoordination and symptoms of pseudobulbar paralysis. These are only some of the conditions described.

The fall in the blood pressure tachypnoea, Cheyne Stokes breathing and even bronchopneumonia and diarrhoea are attributed to lesions of the central nervous system. Ulnar neuritis was observed in 4 per cent. of the cases seen by the author other nerves were less frequently involved.

In early convalescence emotional disturbances lack of power of concentration ataxy and muscular tremors are not infrequent. In elderly and alcoholic patients Korsakoff's syndrome was sometimes observed. Low blood pressure attributable to damage to the vaso-motor centres sometimes persisted for weeks or months after the end of the fever.

John H. D. McGraw

YEOMANS A. SNYDER J. C. MURRAY E. S. ZARAFONETIS C. J. D. & ECKT R. S. The Therapeutic Effect of Para-Aminobenzoic Acid in Louse Borne Typhus Fever. *J Amer Med Ass* 1944 Oct 7 v 126 No 6 249-56 4 charts [Refs in footnotes.]

The authors tried para-aminobenzoic acid in the treatment of 20 cases of typhus fever in the Cairo Fever Hospital of which a special ward was placed at the disposal of the U.S.A. Typhus Commission. Although the number of cases was not large the tests were so carefully controlled that the favourable results constitute strong evidence of the efficacy of the drug. Full details including temperature charts are supplied in respect of 10 cases belonging to the 18-45 age group and of 9 comparable controls consisting of alternate admissions. Altogether there were 17 patients belonging to the above age group whose treatment was started within the first seven days of the illness and 44 control patients comparable in all respects except that the drug was not given. Two patients whose treatment started on the 8th and 9th days and one aged 70 are excluded from the comparison.

The total duration of the febrile period in the 17 test patients averaged 12.5 days and in the 44 controls 18.5 days. The average severity of the illness was much less in the treated. 11 of these had very mild attacks as contrasted with only one of the untreated. Only two of the treated had severe attacks whereas 31 of the controls had either severe (18) very severe (5) or fatal (8) illnesses.

A remarkable feature of the illness among the treated was that in 9 cases there was a secondary rise of temperature varying from a brief subfebrile relapse to one with a moderately high temperature lasting several days. These recurrences of the fever started soon after the end of the course of treatment by the drug none of the patients had severe symptoms the duration of the secondary fever is included in the above estimate of the average duration of the fever among the treated cases.

The results were distinctly more favourable in the patients whose treatment was started early than in those who came under treatment on the 6th or 7th day. No benefit was observed in the two patients treated from the 8th or 9th days onwards. In the patient aged 70 death was probably hastened by the drug which was given to him during collapse and was aspirated into his lung causing acute bronchitis.

A general tendency to leucopenia was observed among the treated in two cases the count fell below 3 000 per cmm. and the treatment was suspended.

The initial dose was 4-8 grammes thereafter 2-0 gm. were given every two hours till the temperature became normal, but the dosage was controlled by frequent estimations of the blood level of the drug the method adopted was one used for determining the sulphanilamide content of the blood.

The para-aminobenzoic acid was given in powder form suspended in a quantity of 5 per cent. solution of bicarbonate of soda sufficient to keep the urine approximately neutral and to prevent vomiting caused by the acidity of the drug.

The urinary output was maintained at 1,500-3 000 cc in 24 hours to prevent high concentration of the drug in the blood, and the toxic symptoms that resulted from this. The optimum dosage of the drug is not yet known. The mode of action was thought to be by inhibiting the multiplication of the rickettsiae and so allowing the natural defences of the body to be mobilized before serious damage could result. The occurrence of the secondary rise of temperature after omission of the drug was thought to favour this view.

The paper contains a table showing the chief data connected with all the treated cases.

The trial of the drug was suggested by the favourable results obtained by SVYDER, MAIER, and ANDERSON (1942) in the treatment of the disease in white mice.

Other reports including the work of ANDREWS, KING, and VAN DEN ENDE [this *Bulletin* 1945 v. 42, 20] were received while the work was in progress.

John W. D. Megaw

LEÓN, A. P. Suero anti tifo de conejos convalecientes en el tratamiento del tifo exantemático. [Antityphus Serum from Convalescent Rabbits in the Treatment of Exanthematic Typhus.] *Rev. Inst. Salubridad y Enfermedades Trop. Mexico*. 1944 June v. 5 No 2, 117-28. [17 refs.] English summary

There were three deaths among 22 patients who were treated for typhus fever by the serum of hyperimmunized rabbits. The ages of the patients are not stated and the author admits that the number treated was too small to justify dogmatic conclusions but he believes that the serum was of decided value. One of the deaths was attributed to a *Salmonella* infection. In the other fatal cases the treatment was started on the 8th or 9th days. The average duration of the fever was 11.1 days. The serum was prepared from rabbits which had received 5-10 intravenous injections of live classical and murine rickettsiae grown in yolk-sac cultures. The blood was collected 10-20 days after the last injection. Great variations were found in the antigenic properties of the different strains as judged by the titre of the Weil-Felix responses in the inoculated rabbits. The most active strains were employed in preparing the sera that were used. Tests of the protective value of the sera were made on guinea pigs—these gave unsatisfactory results but it was believed that rabbit serum was toxic for guinea pigs and that some other animal would be more suitable for use in carrying out the tests.

The treatment was by intravenous injections of doses of 20 cc. given very slowly and repeated 12 hourly till the temperature came to normal or nearly normal. The number of injections needed varied from one to four but the average duration of the illness after starting the treatment is stated to have been 8.2 days. No explanation is given of the discrepancy between these statements.

John W. D. Megaw

BUSTAMANTE M E & VARELA G Características de la fiebre manchada de las montañas rocosas en Sonora y Sinaloa Mexico (Estudio de 12 casos de dos cepas) [The Characteristic Features of Rocky Mountain Spotted Fever in Sonora and Sinaloa, Mexico] *Rev Inst Salubridad y Enfermedades Trop Mexico* 1944 June 16 No 2 129-36 English summary

Between September 1942 and November 1943 12 cases with 10 deaths occurred in rural areas of Sinaloa and Sonora. The probable vector was *Rhipicephalus sanguineus*. All the patients had been exposed to risk of bites by these ticks which infested the numerous dogs of the affected localities. The clinical features were those of virulent types of Rocky Mountain spotted fever. Two strains of rickettsiae were isolated from patients one of these was found by R. R. PARKER to be identical with the Bitter Root Valley strain of Rocky Mountain spotted fever rickettsiae and the other was similar in all essential respects.

LIVESLY H R. & POLLARD, M Serological Studies of Bull's Fever *Amer J Trop Med* 1944 Sept. v 24 No 5 281-4

The authors have already described the isolation of a rickettsia like organism by guinea pig inoculation from the blood of patients suffering from a new fever called Bull's fever [see thus *Bulletin* 1944 v 41 209]. Using an antigen prepared from the spleens of infected mice the authors have carried out a series of complement-fixation tests on sera obtained from 192 former patients two months after the end of the outbreak.

Owing to the sudden disappearance of the infection from the experimental animals it was not possible to carry out the titration of the sera to their end points. Of the sera 147 (78.5 per cent) were positive. 115 of these reacted 4+ at a titre of 1-5 and 32 reacted 2+ at the same titre. 45 were negative. The same sera and 59 others from former patients 261 in all gave negative complement fixation reactions for endemic typhus and negative responses with the Weil-Felix test. One of the sera was positive by serum neutralization test for Rocky Mountain spotted fever.

Control tests were carried out on 29 healthy persons. 4 cases of endemic typhus, 3 cases of Rocky Mountain spotted fever, 2 cases of American Q fever and 4 cases of scrub typhus all were negative for Bull's fever.

Sera of 40 deer (*Odocoileus virginianus* subsp.) shot in the camp area were tested. 4 were positive for Bull's fever and 2 for Q fever. Sera of 7 rabbits (*Lepus californicus*) from the same area were examined. 2 of these were positive for Bull's fever, none for Q fever. The reason for the negative results in 23.5 per cent of the patients is discussed. It may have been the disappearance of the serological sensitiveness of the serum or the inclusion of cases of other diseases mistaken for Bull's fever.

The positive reactions in deer and rabbits from the area suggests that these animals may have become infected at some previous time. An agent has been isolated from *Amblyomma americanum* from the area. This seemed to bear some similarity to the agent isolated by the authors from a human case of the disease.

The conclusion reached is that there does appear to be some significant serological relationship between the agent isolated from a human case of Bull's fever and the serums of convalescent cases.

[It is to be hoped that there will be opportunities for further study of this interesting tick-borne zoonotic fever which clinically resembles fevers of the dengue group rather than those of the typhus group.]

John W. D. Megaw

REUTER A. Ueber das Wolhynische Fieber (Fünftagefieber) [Trench Fever (Volhynian, or Five-Day Fever)] *Mösch. med. Woch.* 1943 Feb. 5 v 90 No 6 99-104 7 charts.

This is a lengthy and somewhat discursive description of trench fever. Apart from the characteristic periodicity of the fever (which was often missing) the chief features of the cases seen by the author were the pains in the joints and shin bones—these were often very severe. Cyanosis of the face, often most easily seen in the lips, occurred in many cases and was a useful diagnostic feature. A rash is said to have been more common than would have been expected from the descriptions of the disease by other observers. It was easily missed because of its appearance only in the earliest stage of the disease. It consisted of red macules distributed all over the trunk and on the limbs.

In one case sudden death occurred soon after an injection of procaine and in another case there was tachycardia with collapse symptoms within an hour of a similar dose. Naturally the use of the drug was promptly abandoned. Suboccipital puncture with the withdrawal of 4-6 cc of cerebrospinal fluid sometimes, though not always, gave relief from severe headache. Massage of the painful parts was badly tolerated in most cases. Strophanthin was of value in cases with cyanosis.

Unlike many of the German physicians who have described the disease during the present war the author regards prolonged convalescence as of frequent occurrence.

John W D Megaw

BURMAN R. Das Blutbild bei Wolhynischem Fieber [The Blood Picture in Trench Fever] *Mösch. med. Woch.* 1943 July 18 v 90 No 28/29 416-18 3 charts

In a series of 25 cases daily leucocyte counts were made. A pronounced leucocytosis occurred in association with the paroxysms of fever in every case the count often rose to 20,000 or more. There was a return to normal or nearly to normal during the afebrile periods but the author states that trench fever can be excluded if no leucocytosis is observed in any of seven consecutive daily counts. There was always a relative lymphocytosis, not infrequently up to 60 per cent. relative lymphocytosis persisted during the afebrile, as well as the febrile periods, throughout the illness. There was seldom any considerable increase in the proportion of the immature neutrophils.

John W D Megaw

REUTER A. & SCHÄFER W. Feldnephritis und Wolhynisches Fieber [War Nephritis and Trench Fever] *Mösch. med. Woch.* 1943 July 30 v 90 No. 30/31 437-40 7 charts

During two winters in Russia the authors saw many cases of illness of which the chief features were oedema and breathlessness, often of short duration fever and shin-bone pains. The blood pressure was seldom raised, and often the urine was normal. The cases ranged in severity from the mild "oedema disease" to typical war nephritis. In some cases the fever had the same periodicity as trench fever. In some cases often occurs. A number of cases are of the same type so that the authors could not find any real line of distinction between the two diseases. The cases are described in support of this contention and the paper is illustrated by seven temperature charts of which four show a 5-7 day periodicity. The authors admit the possibility of the coexistence of the two diseases in some patients but argue, not altogether convincingly, that they were dealing with variants of the same disease.

John W D Megaw

YELLOW FEVER.

STÉFANOPOULO G J & DUVOLOV S Réactivation du virus amaril de culture atténué [The Reactivation of Yellow Fever Virus from Attenuated Cultures.] *Bull Soc Path Exot* 1943 Mar 10 & Apr 14 v 36 Nos 3-4 76-82. [16 refs]

Yellow fever virus when maintained in tissue culture for long periods may show a marked falling off in virulence and also a diminution in its antigenic properties. Thus strain 17 D after being cultured for two to three years in 1938 killed mice only after 15 to 20 days and only in a maximum dilution of 1:10 000. As for its antigenic properties in man this had also diminished and 30 days after vaccination only a very low titre of antibodies was developed. In order to obtain a culture vaccine with better antigenic properties the authors in 1939-1940 passaged the virus through the brains of mice and after six passages the virus killed mice in 7 to 12 days and occasionally was lethal to guinea-pigs. On the other hand this reactivated virus did not become pathogenic to *Aedes aegypti* even after two passages in this monkey although in each case the inoculation was followed by the development of immunity. Attempts to transmit the infection by means of the bites of *Aedes aegypti* were negative but the mosquitoes which fed on the first monkey were found to contain virus which was virulent to mice.

The reactivated virus was again cultivated successfully in the embryonic tissues of incubated eggs. The virus of the first and second passages in eggs killed mice in 8 to 12 days. A vaccine prepared from this virus was used for the vaccination of 102 human subjects comprising 80 males and 22 females and including 5 infants from 10 months to 8 years of age. Post vaccinal symptoms were very slight. 15 persons had a slight fever between the 4th and 8th days but in only 5 cases did the temperature reach 38.5°C (101.3°F). Protection tests were carried out on 26 of these patients after an interval of 3 to 4 weeks. Eleven were strongly positive, 13 positive and 2 negative.

E Handle

DENGUE

DIASIO J S & RICHARDSON F MacD Clinical Observations on Dengue Fever Report of 100 Cases. *Milit Surgeon* 1944 June v 94 No 6 365-9

The authors like many other physicians on their first encounter with dengue were struck by the great variations that occur in the disease even within the limits of a single epidemic. They have analysed the symptoms and signs observed in 100 consecutive patients somewhere in the South Pacific area probably in Australia.

The percentage incidence of some of the chief features was as follows: Head-ache 94, backache 89, pains in legs or joints especially the knee joints 75, pain on movement of eyeballs 74, chill at onset 14, chill, not at onset but within 12 hours 40, insomnia 53, weakness especially of legs 29, when this was complained of it was usually the first symptom, indefinite feeling of coryza 24, always before the onset and never persisting, fleeting soreness of the throat with the coryza 12. The temperature fell to or nearly to normal within 2-3 days in most cases, at the same time the symptoms subsided and the rash faded about two days later, the fever symptoms and rash returned but the second spell of fever was shorter and less severe than the first. There was itching of the palms and soles after the final fall of the temperature in 17.

20 patients. Scleral injection was seen in 89 cases and was the most characteristic of the early signs. In 57 cases pin-point vesicles were observed on the posterior part of the soft palate. These first appeared within about 12 hours of the onset, soon they became red and with their gradual disappearance the area of redness reached a pin-head size by the 2nd or 3rd day of the fever. The spots resembled the mucous-membrane rash of rubella. There was no return of these spots during the second spell of fever.

The skin rash was quite different from that usually described. In 79 cases a morbilliform rash was seen on admission. Sometimes this took the form of discrete pink spots on the sides of the chest, inner surface of the upper arm, and lumbar region. In severe cases there were erythematous areas on the lower part of the face on the neck, shoulders and thorax. The rash faded during the afebrile period, and recurred, though less intensely with the second rise. In 11 cases the rash was absent during the first spell of fever but appeared during the second.

In 33 patients the face was flushed and swollen at the onset. Adenitis was a prominent feature. The posterior cervical glands were enlarged in 84 cases the epitrochlear in 90 and the inguinal in 80.

A typical "saddle-back" fever curve occurred in 53 cases. There was a single spell of fever ending by lysis in 2-7 days in 33. The curve in the remaining 12 cases were irregular in type. The leucocyte count ranged from 3,600 to 10,000 per cmm. in the cases examined on the first day. The average count on admission was 5,450 and on the 5th day it was 3,500. *John W. D. Megaw*

BACILLARY DYSENTERY

WINTS C. W. Jr & TALLANT E. J. Dysentery in American Troops in the Middle East. *Amer J Digestive Dis* 1944 Aug., v 11 No 8, 252-5

Between January and August 1943 stools from 1,298 individuals belonging or attached to the American Forces in the Middle East were examined macroscopically and microscopically and were cultured on desoxycholate-citrate agar or on eosin methylene-blue agar. Among 300 normal controls, intestinal parasites (protozoa and worm-ova) were isolated from 1 per cent. of 200 American soldiers (all food-handlers) from 4 per cent. of Sudanese soldiers and from 98 per cent. of native workmen while bacterial pathogens (Morgan's bacillus is included in this category) were recovered from 1.5 per cent. of the American soldiers and from 4 per cent. of the Sudanese soldiers and native workmen. No pathogens were isolated from 6 lots of flies. Among patients with intestinal symptoms, 118 (12 per cent.) harboured intestinal parasites. *E. histolytica* was recovered from 9 patients, of whom 8 had clinical dysentery. Hookworm infection was found in 5 patients. Bacterial pathogens were isolated from 238 patients (23 per cent.). The predominant organism was *Bact. flexneri* (including *Boyd 88* or the *Verocelle* variant) isolated from over 60 per cent. of the positive cases. salmonella organisms (including the paratyphoid bacilli) were recovered from 17.5 per cent. *Bact. shigae* from 3 per cent. and Morgan's bacillus from 9 per cent. The dysentery infections were of moderate severity. 60 per cent. of the patients had blood and mucus in the stools. They responded well to sulphaguanidine. salmonella infections did not. Among 300 patients with negative stools, the final clinical diagnosis was mostly of diseases other than intestinal infections.

The authors deprecate the diagnosis of "Gypsy tummy" as if it were a mysterious intestinal infection of non specific origin to which most newcomers

to the Middle East fall victim. They quote evidence that this condition—characterized by fever, malaise, abdominal cramps and diarrhoea for 2–3 days—is often due to organisms of the dysentery group. *Robert Cruickshank*

BOSE A. N. & GHOSH J. K. Studies on Sulphanilyl-Benzamide. Toxicity and Absorption. *Indian J Med Res* 1944 May v 32 No 1 61–3 [11 refs.]

Sulphanilylbenzamide was described by BROWNLEE and TOWNIN [this *Bulletin* 1942, v 39 35] as having properties which might make it more effective in the treatment of bacillary dysentery than sulphaguanidine. It is very insoluble in water. When emulsions were injected into mice intravenously or intraperitoneally the highest doses employed (1.5–2.0 mgm per gm) rarely caused death. When 0.5 mgm per gm. was given to mice orally, the maximum blood concentration was 25 mgm free drug per 100 cc. and 33 mgm total drug. It is absorbed fairly rapidly from the alimentary canal of mice. [The reviewer (*Lancet* 1942 Mar 7 290 *Bulletin of War Med* 1942 v 3 41) found that following oral administration the concentration of sulphanilylbenzamide in the faeces was comparatively low.] *F. Hawking*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

MANSON BAHR P. Amoebic Dysentery. Facts and Fallacies in Radical Treatment. *Lancet* 1944 Dec. 2 718–20 [29 refs.]

The author finds it disturbing that the apparently well founded views of those with long experience of the treatment of tropical disease are being called in question by medical officers of limited experience of these conditions. He quotes the treatment of amoebiasis as a case in point and observes that after the unduly optimistic early reports on the employment of emetine in *E. histolytica* infections had been tempered by experience and by the acquisition of further knowledge of the life-cycle of the parasite it was evident that injections of emetine hydrochloride, however large in amount and however prolonged, exerted no recognizable effect on the chronic infection or on the symptoms caused by it—important basic facts apparently not appreciated by many now treating the disease. Emetine given by injection is presumably distributed in the blood stream and it does not reach the precystic amoebae which congregate on the mucous surface of the bowel and which can be extirpated only by drugs introduced directly into the alimentary tract. E.B.I. (emetine-bismuth iodide) introduced in 1915 was found to be an effective drug against these forms when given orally and after the 1914–18 war many pensioners were permanently cured of their infections by it. Some however (about 12 per cent) were resistant to it and these were chiefly cases which had been subjected previously to a long series of hypodermic emetine injections. Continued intensive E.B.I. treatment is useless in such cases but most of them are curable by chiniofon (B.P.), a combination of iodine with oxyquinoline-sulphonic acid first used in amoebiasis by MÜHLENS and MENK in 1921 [this *Bulletin* 1922, v 19 31]. Chiniofon is more effective when given as a rectal retention enema (in 2.5 per cent. solution) than by the mouth but the author found in 1925 that about one-quarter of a small series of E.B.I. resistant cases were not cured by chiniofon given simultaneously by mouth and rectally.

In view of this in 1926 [this *Bulletin* 1932 v 29 581] he elaborated his method of combined treatment with the two most specific anti amoebic drugs—E.B.I. and chiniofon—described in detail in recent editions of his *Tropical*

Diseases and Dysenteric Disorders. The author re-emphasizes the importance of attention to detail and to certain precautions in the administration of the drugs, and he draws attention to some reasons for the occasional apparent failure of the treatment—this may be due to giving the E.B.I. in insoluble coated tablets preventing the liberation of the drug in the small intestine, or to the mal-administration of the retention enema of chiniofon so that the latter becomes merely a washout, and is neither retained nor distributed throughout the large intestine. A case of allegedly resistant *E. histolytica* infection of long standing is cited, which yielded to his treatment after protein shock therapy.

After reference to the arsenical preparations acetarsol and carbarsone and to "Enterovioform and Diodoquin"—to none of which does he attach much virtue—the author deprecates the common practice of giving all these drugs in futile and wearisome succession. He reaffirms that the periodic administration of courses of emetine is injurious and should be discouraged, E.B.I. and chiniofon properly given together offering the best hope of permanent cure.

A. R. D. Adams

TAUBENHAUS L. J. Amebiasis as Cause of Recurrent Abdominal Pain. Report of Cases. *U.S. Nav. Med Bull.* 1944 Sept., v 43 No. 3 527-31

Patients complaining of recurrent abdominal pain, not always associated with diarrhoea, present a problem in diagnosis and treatment. The results of clinical examination may vary from absence of physical signs to tenderness over part of the colon, and the blood findings from a normal count to a leucocytosis of 20 000 per cmm. Some of these patients appear ill, others perfectly well, some are eventually diagnosed as having appendicitis and the appendix is removed, but the patient "invariably returns with a recurrence of his symptoms." Many complaining of fatigue and weakness are apt to be dismissed as neurotics or malingerers. For six months routine proctosigmoidoscopic examination has been carried out at several U.S. Naval dispensaries on all patients complaining of recurrent abdominal pain, except those in whom a definite diagnosis of appendicitis or peptic ulcer could be established. In a very large number a diagnosis of amoebiasis has been made. The practice of routine examination of five stools prior to sigmoidoscopy was abandoned as unsatisfactory as it was found that proctosigmoidoscopy sufficed to establish the diagnosis.

Sigmoidoscopic appearances of the amoebic lesion varied from minute, red, punctate ulcers which appear as pin-pricks in the mucosa to the typical, larger irregular undermined ulcers with necrotic bases. The majority of lesions are found on the rectal valves or on the anterior rectal wall distal to the lowest valve. Minute punctate lesions may easily be overlooked, and are best seen as the instrument is being inserted—in some patients, however the rectal mucosa had a granular appearance similar to that of early nonspecific ulcerative colitis. The diagnosis can be established only by finding the actual amoebic lesion containing either the motile or cystic forms of *Entamoeba histolytica*. This is best effected by examining fresh scrapings made from the edges of the ulcers suspended in normal saline. Cleansing the bowel thoroughly with a tap-water enema is sufficient preparation for proctosigmoidoscopy and more satisfactory than other types of cleansing enemas. Contrary to popular misconception amoebiasis is not a disease of the tropics and subtropics only. The patients involved came from all parts of the U.S.A. and careful history taking elicited the fact that in most cases symptoms were present before enlistment.

The symptoms varied considerably but in all cases, except one, there was a history of diarrhoea at some time and all the patients complained of abdominal pain—in most, it was recurrent cramp-like and difficult to localize. The only

constant sign was tenderness over some part of the colon and only in those with actual dysentery was there any blood in the stools. There was no correlation between the degree of rectal involvement (as seen through the sigmoidoscope) and the clinical picture. Some with mild symptoms had widespread rectal involvement whereas one with dysentery had only a few minute punctate ulcers. There did however seem to be a relationship between the scrapings of the ulcers and the finding of motile or cystic forms of *E. histolytica* in the scrapings whilst in those in whom pain and not diarrhoea was the outstanding symptom the cystic form predominated. The question whether dysentery or the milder type of infestation results seems to depend on the resistance of the host thus amoebiasis may present a clinical syndrome different from that of amoebic dysentery.

The author concludes that probably any adequate specific therapeutic regime will suffice to cure these cases. Treatment usually consisted of a course of emetine injections followed by successive courses of carbarsone, viofilm and yet more carbarsone.

ATWELL A G & BAILEY N. A Case of Amoebic Cystitis. *South African Med J* 1944 Oct 14 v 18 No 19 335

The case described came under observation for burning sensation during micturition. Examination of the urine revealed red blood corpuscles epithelial cells and a few pus cells as well as actively motile *E. histolytica* some of which contained red blood corpuscles to the number of seven. Amoebae were again observed two days later but many were rounding off and dying while others were sluggishly motile. The following day further signs of degeneration of the amoebae were noted while a flagellate was seen. After two more days nothing abnormal could be detected. The patient was sent to hospital where amoebae could not be detected though *Trichomonas hominis* was found. Investigation showed that the inflammation was confined to the bladder and did not extend to the ureter or kidneys. The urinary condition shown to be due to *Bact coli* cleared up on treatment with sulphonamide.

VERSIANI V & RENAULT L. Incidencia da *Giardia lamblia* em Belo Horizonte [Incidence of *G. intestinalis* in Belo Horizonte] *Brasil-Médico* 1944 Aug 19 & 26 v 58 Nos 34 & 35 322-4

RELAPSING FEVER AND OTHER SPIROCHAETOSSES

MARQUES A. Tick Spirochaetoses or Non-Epidemic Relapsing Fever at Xinauane. *South African Med J* 1944 Nov 11 v 18 No 21 360-64

The author reviews the clinical histories of cases of tick fever observed at Xinauane Lourenço Marques and calls attention to the extraordinary diversity of symptoms which may simulate the most varied diseases ranging from malaria broncho-tracheitis and dysentery to orchio-epididymitis epilepsy and even obesity. The necessity for blood examination in order to arrive at a correct diagnosis is evident and the author recommends the use of thick films stained with Leishman's stain. No satisfactory results were obtained by the use of organic arsenicals such as neoarsphenamine and the author now limits himself mainly to symptomatic treatment.

The normal vector *Ornithodoros moubata* is widespread but it is particularly desirable that all buildings occupied by successive gangs of Africans should

be disinfested. The author recommends plastering the floor and walls with cement leaving a hollow groove about a yard above the floor level to act as a hiding place for ticks. During the day this groove can be gone over with a blow-lamp or sprayed with an insecticide such as "Destructine No. 2," or "Pyrethra" diluted with 9 parts of paraffin.

The author gives figures showing the early records of sickness, etc., on the Incomati Estates. These figures indicate a decline in the general sick-rate after the introduction of plastering in 1943 and also supports the view that tick fever is one of the most important diseases among African labourers in this district.

E. Hindle

HUME, W. E. & SZEKELY, P. Cardiac Involvement in Spirochaetal Jaundice. *Brit. Heart J.* 1944 July v 6 No 3 135-8 2 figs. 21 refs.]

The authors review the available papers dealing with cardiac complications of spirochaetal jaundice and then give details of a case.

The patient a seaman aged 52 years had fallen into the Thames 10 days before the onset of symptoms. He was admitted to the Newcastle General Hospital 10 days later and was then deeply jaundiced. His serum agglutinated *L. icterohaemorrhagiae* in titres up to 1:30,000 and the clinical features were typical of the disease. On the 13th day of illness the heart rhythm was found to be irregular and a cardiogram showed the presence of auricular fibrillation. The myocardial involvement was only transient and in the light of anatomical findings in fatal human cases and in infected guinea-pigs it is considered to be the result of multiple haemorrhages or of direct toxic damage to the heart muscle or both.

E. Hindle

ALSTON, J. M. & BROOK, J. C. The Action of Penicillin on *Leptospira* and on Leptospiral Infections in Guinea-Pigs. *Brit. Med. J.* 1944 Dec. 2, 718-19

The authors tested the effect of penicillin on the growth of leptospirae in culture and on leptospiral infections in guinea-pigs.

Nine strains of *Leptospira icterohaemorrhagiae* were used, including six human strains, two from rats and one from a dog, and also a strain of *L. canicola*. The growth of all these strains was prevented by adding penicillin in concentrations of 0.4 Oxford unit to 3.5 cc. culture medium before seeding with 0.25 cc. of a heavy culture of leptospira. With lower concentrations variation of sensitivity was found. In well grown cultures the addition of penicillin in concentrations of less than 15 Oxford units in 10 cc. had no apparent effect on leptospira and even in concentrations up to 240 Oxford units the organisms although greatly diminished were not entirely eliminated after three weeks' contact at 24°C.

Fifteen guinea-pigs were inoculated intraperitoneally with a virulent strain of leptospira. 7 were treated with sodium penicillin in oil, begun 18 hours after infection, and 8 were left as controls. Each treated animal received a total of 12,000 units extending over 15 days equivalent to more than 1,000,000 units for a man of 70 kgm. Four out of 8 control guinea-pigs survived and 6 of the 7 treated animals. Serum of all guinea-pigs recovered after penicillin treatment agglutinated *L. icterohaemorrhagiae* in dilutions of 1:30 or 1:100. Ten were re-inoculated without showing any signs of infection.

Finally, the authors tested the toxicity of penicillin in guinea-pigs. Six normal animals were given 800 units of sodium penicillin daily for 15 days, and three weeks later 1,100 units twice daily for three and a half days, without any ill effects being observed, in opposition to the results recorded by HAMRE *et al* (*Bulletin of Hygiene* 1944 v 19 310) and also HELLMAN and HERRELL (see this Bulletin 1944 v 41 1039).

E. Hindle

HART V L. A Case of Weil's Disease treated with Penicillin *Brit Med J*
1944 Dec. 2 720

The patient an Italian male aged 26 who had worked in ditches and canals developed a typical attack of Weil's disease diagnosis being confirmed by agglutination tests and the appearance of *Leptospira* in the alkaline urine on the 23rd day of the illness. They were still present on the 30th day when penicillin treatment was begun. 15 000 units every four hours continued until 315 000 units had been given. The penicillin did not seem to hasten recovery but the organisms disappeared from the urine two days after treatment had begun.

E Hindle

YAWS AND SYPHILIS

YOUNG W A. Extra-Urethral Cases in an African Venereal Diseases Hospital.
Brit J Venereal Dis 1944 Dec 1 20 No 4 141-54 [20 refs]

No adequate abstract of this article is possible within a limited space and those who are interested are recommended to study the original in detail.

The author's theme is to show how common syphilis yaws chancre and lymphogranuloma inguinale are in Africans their relative incidence in East and West Africa the impossibility of differential diagnosis and in consequence the difficulty of prescribing suitable treatment. Further the difficulties are increased by the added complication of filariasis.

A series of 222 cases of venereal disease other than gonorrhoea is analyzed and of these no less than 49 (22 per cent) showed some degree of positivity with the Kahn Ito-Reenstierna and Frei reactions. 104 (47 per cent) gave positive results with two reactions, but only 24 (11 per cent) had a positive Kahn reaction alone and 38 (17 per cent) positive Reenstierna reaction alone. Only one man had a positive Frei without a positive Kahn or Reenstierna. These facts give some idea of the complexity of the matter and this complexity was increased by the fact that one locally made Frei antigen appeared to act as Ducrey antigen as well.

Sores were so frequently due to more than one infection that differential diagnosis was virtually impossible whatever their characters. Separation of the various diseases according to the condition of the lymphatic glands seemed a little more hopeful in general adenitis and periadenitis are characteristic of syphilis periadenitis especially when it extends to the skin is characteristic of chancre and cutaneo-periadenitis is characteristic of lymphogranuloma inguinale. This last was the only disease which could be identified with any degree of accuracy and was thought to constitute approximately 10 per cent. of the whole series.

From the foregoing it will be realized that treatment also presents a problem. The author considers that taking all the factors into consideration especially the butterfly out patient treatment should be as intense and short as possible and that simultaneous short courses of mapharside sulphapyridine and tartar emetic are the only practicable solution.

[No mention is made of granuloma venereum (granuloma inguinale) which may perhaps complicate matters further. Some might consider that in the treatment of Africans sulphanilamide is more suitable than sulphapyridine for chancroid and be led to wonder whether tartar emetic has much effect on L.i.]

T E Osmord

are acid fast. The authors state that they have occasionally even seen spores. If transferred again from 4 to f the acid fast bacillary form is resumed. These different forms are shown in a coloured plate. *H Harold Scott*

ARGÜELLES CASALS, D. *Lepra y xantelasma*. [Leprosy and Xanthelasma.] *Rev Leprologia Dermatología y Sifilografía* Marianao Cuba. 1944 Oct. v 1 No. 4 242-4

The association of these two conditions in the same patient states the author has been observed fairly often but no allusion to it is made in the text books. It seems to occur in lepromatous cases in later middle age and if autopsy is undertaken lepromous lesions are often found in the liver. The author cites three cases under his observation. In a woman of 68 another of 59 and a man of 65 years these were all among 33 lepromatous patients examined. It was not seen in 22 others of the tuberculoid or non-specific types. The fact that hypertrophy of the liver is common in leprosy without disorder of liver function is ascribed to the infiltration affecting the periportal spaces and not the cellular structure of the organ. *H Harold Scott*

POIRIER, M. Note sur 15 cas de lèpre observée au service des contagieux du Val-de-Grâce chez des Sénégalais. [Fifteen Cases of Leprosy in Senegalese Soldiers seen at Val-de-Grâce.] *Bull Soc Path Exot* 1943 May 12 & June 9 v 36 Nos 5-6 145-6.

ROIG J T & RODRIGUEZ DE LA CRUZ J M. Los aceites de las flacurciáceas sus propiedades. Aceites de las flacurciáceas Cubanas. [The Essential Oils of the Flacurciaceae and their Properties. The Oils of Cuban Species.] *Rev Leprologia, Dermatología y Sifilografía*. Marianao Cuba. 1944 Oct. v 1 No. 4 256-66 [16 refs.]

By properties the authors imply the physical characters not the therapeutic uses, of the various plants. They give the specific gravity at certain temperatures the refractive index the rotatory power the index of saponification etc. of the twelve chief species of *Taraktogenos* and *Hydnocarpus* (among the latter *wightiana anthelmintica alcalis kutchinasonis thiofolia woodii* and *subfalcata*) and then give the same information regarding the species which flourish in Cuba namely *Guaguani* oil, *Zuelania guidonis* oil of Ranilla, *Lactia americana* oil of Rascabarriga, *Samyda grandiflora* oil of Jia blanca from the seeds of *Casearia alba* and of *Raspalengua* obtained from *Casearia hirsuta*.

The oils of these three genera *Zuelania* *Lactia* and *Casearia* are very similar to those of *Hydnocarpus* *Lindackeria* and *Carpotroche* and in all of the Cuban plants gynocardic chaummoogric and gerlic acids are present. Moreover as far as they have been tried, the esters of these Cuban oils are well tolerated when injected intramuscularly and a plea is made for more extensive trial of them and for publication of the results observed. *H Harold Scott*

IBARRA PEREZ, R. & GONZALEZ FREYRE, M A. Las sinomias de la lepra. [Synonymy in Leprosy.] *Rev Leprologia Dermatología y Sifilografía*. Marianao Cuba. 1944 Oct. v 1 No 4 267-75 [26 refs.]

VILLILA, G G & LINHARES, H. Lipídeos na pele de ratos com lepra murina. [Skin Lipoids of Rats with Rat Leprosy.] *Mem. Inst Oswaldo Cruz*. 1943, Feb v 38 No. 1 61-4 English summary

HELMINTHIASIS

WRIGHT F J & ROBERTS J I A Creeping Eruption with Intense Eosinophilia in a Case of Infection by *Schistosoma mansoni* *East African Med J* 1944 Sept v 21 No 9 282-4 1 chart

During the early period of infection with *Schistosoma mansoni* a linear creeping eruption appeared in the skin of an Indian boy aged nine years he had paddled in Nairobi river [Kenya Colony] on March 29th 1943 and next day had red and swollen legs up to the knees which he scratched owing to the irritation. On the third day after the paddling he vomited and had fever which recurred intermittently in spite of treatment at a dispensary until his admission to hospital on April 20th three weeks after paddling. He showed oedema of the face spasmodic cough at night and urticaria on the thighs and legs. On April 24th a somewhat wavy semicircular line about 6 inches long appeared on the left thigh it was raised red and irritable but not painful or tender. The line grew between 9 a.m. and 2.30 p.m. at the rate of 2 inches an hour. Two other semicircular lines one beginning as an urticarial weal appeared about the same time on the right thigh. These lines were sprayed with ethyl chloride and no further extension or urticaria appeared.

The stools showed ova of *S. mansoni* for the first time on May 5th 1943 though examined several times a month they were only found again once in August and again in March 1944 during this period several courses of injections with antimony compounds were given.

In May 1943 the blood contained 63 600 leucocytes per cmm. of which 60 800 (95.6 per cent) were eosinophils. The leucocytosis gradually decreased during the following months to reach 10 000 in March 1944 the eosinophilia showing a parallel curve of decrease.

J F Corson

LE GALL, R. Les bilharzioses en Afrique Occidentale Française au Togo et à Madagascar de 1939 à 1941 (*Schistosomiasis in French West Africa, Togo and Madagascar, 1939-41*) *Bull. Office Internat. d'Hyg. Publique* 1944 Mar-Apr v 36 Nos. 3-4 116-26 8 maps.

- i TÖTTERMAN G. Anemia Hyperchromica Diphyllobothrica. *Acta Med Scandinavica* 1944 v 118 No 4-5 402-9 [11 refs.]
- ii — On the Occurrence of Pernicious Tape-Worm Anemia in Diphyllobothrium Carriers. *Ibid* 410-16 [11 refs.]
- iii — Experiments with Injections of Stomach Extracts in Pernicious Anemia. *Ibid* 417-21 [15 refs.]
- iv — Furthermore on the Question of the Pathogenesis of Pernicious Tape-Worm Anemia. A Preliminary Report. *Ibid* 422-9

i In the first of these four papers the author reminds us that *D. latum* may cause in a fraction of the number of carriers of this tapeworm a disease which is indistinguishable from cryptogenetic pernicious anaemia and that both diseases are improved by liver and stomach preparations. Other anaemias have been ascribed to *D. latum* e.g. a hypochromic type of which the author saw 10 cases none of which was improved by anthelmintic treatment so that he concluded that probably *D. latum* does not cause this kind of anaemia and a light hyperchromic anaemia sometimes almost normochromic (anaemia hyperchromica diphyllobothrica) which does improve after anthelmintic treatment without any other treatment. This latter anaemia was described by G. BECKER (*Finska Läk. sällsk. Hdl* 1915 v 57 513) and by TÖTTERMAN [this *Bulletin* 1940 v 37 215]. The present paper records the study of 24

cases of this kind of anaemia (15 women, 9 men) all adults. The anaemia in all was very moderate. In the 15 women the haemoglobin percentage was 72-86 average 83 the erythrocytes numbered 3 430 000 to 4 378 000 average 3,949 000 the colour index was 1.01 to 1.10 average 1.05. In the nine men the haemoglobin percentage was 68 to 100 average 87 the erythrocytes numbered 3 110 000 to 4 600 000 the colour index was 1.00 to 1.12, average 1.08. Gastric acidity was normal and there was no connexion between the secretion of HCl and the anaemia.

A vermifuge was given to 12 of the 24 patients and the blood picture became normal "in some weeks" without other treatment. To the other 12, injections of a liver preparation called Heptornum Medica were given in doses which had caused complete improvement of the blood picture in cases of pernicious anaemia. In one of these 12 cases all traces of the anaemia disappeared in one month; in five of them there was a distinct, but not a complete improvement but a vermifuge did improve them. In the remaining six cases the liver preparation appeared to have no effect upon the anaemia but in four of them a vermifuge noticeably improved the blood picture. If this hyperchromic anaemia had been a primary stage of tapeworm pernicious anaemia as RAGOZA (*Fol haemat. Archiv* 1915 v 19 266) has suggested, the liver preparation should have been, Tötterman argues at least as effective in these cases as it is in tapeworm pernicious anaemia. The author thus concludes that this light hyperchromic anaemia and tapeworm pernicious anaemia are not different stages of the same disease, but are distinct conditions. The light hyperchromic anaemia is perhaps due to absorption of tapeworm toxins and is comparable to experimental poison anaemias in animals. The absorption of tapeworm toxins will not alone cause tapeworm pernicious anaemia other factors must collaborate to produce this. This explains why tapeworm pernicious anaemia is so much less frequent than light hyperchromic anaemia.

ii. In the second of these four papers the author discusses the literature on the occurrence of tapeworm pernicious anaemia in carriers of *D. latum* and gives the results of his own study of its incidence. EHRSTROM R. (*Finska Läk sällsk. Hdl.*, 1928 v 68 685) calculated that tapeworm pernicious anaemia will occur in only 1 in 5,000 to 10,000 cases of infestation with *D. latum* but he based these figures on estimations made by provincial doctors and Tötterman thinks that the figures are very unreliable. SEPPÄ, T. (*Duodenum* 1927 v 43 101) examined patients admitted to a military hospital and found a proportion of one case of tapeworm pernicious anaemia in 639 cases of infestation with *D. latum*. SCHAUMAN O. (*Åkad Åbb Helsingfors*, 1894) studying clinical material, gave an incidence of one case in 100. BECKER, G. (*Finska Läk sällsk. Hdl.* 1915 v 57 513) gave an incidence of one case in 168 these figures being based on his private practice. Both the latter authors thought however that their figures were too high.

Tötterman studied civilians and soldiers admitted to a war hospital during the 18 months between July 1st 1942, and December 31st 1943. In 1942 the stools of practically all the patients were examined but in 1943 they were not as a rule examined. In the second half of 1942 *D. latum* was found in 151 of 850 military patients (17.8 per cent) and in 154 of 233 civilians (66 per cent.) in "polyclical material" comprising 273 civilians *D. latum* was found in 113 (41.4 per cent). In 1943 *D. latum* was found in 275 of 1,896 military subjects (14.5 per cent.) and in 245 of 410 civilian subjects (59.75 per cent.) and in 209 out of 379 polyclical civilians (55 per cent). Tötterman thinks that the 14.5 per cent. incidence in the 1943 military patients is almost an exact fact for the Finnish Army because the subjects examined came from all over that country and that 14 per cent. is an approximate mean value for the incidence over the whole of Finland.

Discussing the diagnosis of tapeworm pernicious anaemia Tötterman states that it must be hyperchromic and also very pronounced [contrast the moderate anaemia in the first paper] and must respond to treatment with liver preparations or by expulsion of the worm. During the latter part of 1941 15 cases of tapeworm pernicious anaemia were treated and the author gives figures from which he calculates that the frequency of tapeworm pernicious anaemia was 1 138 among civilians and 1 113 among soldiers. In 1942 there were fewer cases occurred. The incidence then was 1 383 among civilians and 1 281 among soldiers. These figures represent the author's estimate of the true incidence. He is inclined to ascribe the higher frequency of the anaemia in 1942 to the difficult food conditions in that year and perhaps also the lack or scarcity of Castle's extrinsic factor. During the war KERPPOLA (personal communication to the author) obtained good results by treatment with yeast which is rich in extrinsic factor. The author considers that his own figures obtained during a time of food difficulty may be the highest possible while STENFELT's figure of 1 659 obtained from the study of conscripts in normal times may be the lowest possible.

iii. In the third of these four papers the author discusses earlier work on the use of intramuscular injections of gastric juice for pernicious anaemia. For this treatment excellent results have been claimed. He also discusses the use of injections of stomach extracts. He describes his own method of making extracts of hog's stomach. Two extracts of the fundus of the stomach only were given intramuscularly to one case of cryptogenetic pernicious anaemia and to one case of tapeworm pernicious anaemia. No improvement resulted in either case. Five extracts were made from hog's stomach from which the fundus had been removed. These were injected in large doses into five patients with cryptogenetic pernicious anaemia and into one with tapeworm pernicious anaemia. Four of the cases of cryptogenetic pernicious anaemia did not improve. One case improved slightly. When the extracts made without the fundus were given by the mouth to one patient with cryptogenetic pernicious anaemia also improved slightly. When the extracts made without the fundus were given by the mouth to one patient with cryptogenetic pernicious anaemia 15 gm. were given four times a day for 10 days) no improvement resulted. These negative results are contrary to those obtained by some of the earlier investigators whose work is discussed.

iv. In the fourth of these papers the author supports the view that tapeworm pernicious anaemia occurs in patients who have become sensitive to the tapeworm. He had previously found (presumably *Acta med scand* 1938 v 96 268) that when patients who had had tapeworm pernicious anaemia were given small doses by the mouth of dried tapeworm or alcoholic extracts of them the blood picture declined in the direction of pernicious anaemia. This did not seem to occur in healthy subjects or in cases of cryptogenetic pernicious anaemia. Tötterman discusses von BONSdorff's criticism (this *Bulletin* 1940 v 37 216) of this view pointing out that von BONSdorff used for his work chiefly aqueous extracts of the tapeworm whereas Tötterman insists that they must be alcoholic.

To study the problem further Tötterman extracted *D latum* for one week with equal parts of ether and 96 per cent. alcohol filtered the extract and evaporated it slowly on a water bath. The residue was suspended in almond oil and sterilized in a water bath. Each gramme of this almond oil extract contained the extract from 10 gm. of tapeworm. Each dose of it given daily by intragluteal injection was 0.5 cc.

Case 1 had no anaemia and no *D latum*. He was given 0.5 cc. of the extract daily for 19 days. The haemoglobin and number of erythrocytes did not increase the eosinophils rose from 1.5 to 7.5 per cent.

Cases 2 and 3 had no anaemia but had *D. latum*. Case 2 received 0.5 cc. of extract daily for 14 days and showed slight decrease of both haemoglobin and number of erythrocytes but these both improved again later although the injections continued. The eosinophils increased somewhat. Case 3 received 0.5 cc. almost daily for five weeks. During the first three weeks the haemoglobin decreased from 87 to 85 per cent. the erythrocytes decreased from 4,790,000 to 3,960,000 but both increased again later although the injections were being continued. The eosinophils increased up to 17.5 per cent.

Case 4 had typical tapeworm anaemia which had been completely cured by anthelmintic treatment. Given 0.5 cc daily for 12 days the haemoglobin of this patient decreased with 16 per cent and the erythrocytes with 1 million in two weeks the colour index and eosinophils were not changed. The injections were discontinued because of the deterioration of the patient's condition the blood values then rose until in three weeks, they were the same as they had been at the beginning.

Case 5 had recovered two months earlier from tapeworm pernicious anaemia after anthelmintic treatment. Given 0.5 cc of extract daily for 15 days this patient showed a decline of haemoglobin from 101 to 90 per cent. The erythrocytes declined rather more than 700,000. The colour index rose from 1.01 to 1.07 and the eosinophils from 2 per cent to 17.5 per cent. The injections were discontinued and in three weeks the patient's blood picture improved spontaneously and the eosinophils returned to 5 per cent. Another test was done with a new extract made by dissolving the ether-alcohol extract in petrol ether evaporating the petrol-ether and suspending the residue in almond oil a pure lipid extract being thus obtained. For two weeks the patient received 2 cc. of this daily. The haemoglobin was reduced from 97 to 94 per cent the erythrocytes by 300,000 the colour index rose from 1.01 to 1.04 and the eosinophils from 5.5 per cent to 10.5 per cent.

NYFELDT using *Bothriocera* found that when constant doses were used, the blood changes gradually disappeared as they did in cases 3 and 4 above only when the doses were continually increased did NYFELDT find some hyperchromic anaemia in the animals he used. TALLQVIST took by the mouth increasing doses of tapeworm lipoids and caused hyperchromic anaemia. TÖTTERMAN suggests that the increase of eosinophils obtained by him indicated that the tapeworm toxins in his extracts were genuine. He concludes that his results correspond well with his earlier results obtained by giving by the mouth small doses of dried *D. latum* or alcoholic extracts of it and that they support his earlier conclusion that hypersensitiveness to *D. latum* toxin plays an important part in the pathogenesis of tapeworm anaemia.

G. Lapege

O'CONNOR, N. Infestation by Two Types of Tapeworm. [Correspondence]
Brit Med J 1944 Dec 2 737

A man and his wife who had lived for many years near the River Erne Ireland were infested with *Diphyllobothrium latum* and the wife was also infested with *Taenia saginata*. Both habitually ate perch pike and eels but not trout, and the wife frequently ate under-cooked meat and raw pork. After receiving anthelmintic treatment the man passed a worm 11 feet long and his wife passed a mass of worms in which one head of *T. saginata* and 35 heads of *D. latum* were found. Blood films of the man were normal while those of his wife showed 11 per cent. of eosinophilic leucocytes. The author gives references to other records of infestation with *D. latum* in Ireland, all of which were in the county of Letchim near the River Shannon [this *Bulletin* 1918 v 12, 191 1931].

v 28 200 *Lancet* 1916 Feb 26 466 *Irish J Med Sci* 1929 6 ser 95 *Ibid* 1935 6 ser 188. See also this *Bulletin* 1944 v 41 857 & 859] *J F Corson*.

v HOLLÓSY K. Spulwürmer als Ursache der Darmperforation. [Nematodes as a Cause of Intestinal Perforation.] *Zeits f Chirurgie* 1942 Dec. 19 v 69 No 51 1990-92

LASER H. The Oxidative Metabolism of *Ascaris suis* *Biochem J* 1944 v 38 No. 4 333-8 10 figs. [21 refs.]

OLIVER-GONZÁLEZ J & BERCOVITZ Z T. Precipitin Reactions with Antigen prepared from Microfilariae of *Wuchereria bancrofti* (Preliminary Report) *Amer J Trop Med* 1944 Sept v 24 No 5 315-16

An antigen was made as follows from the microfilariae of *Wuchereria bancrofti*: citrated blood containing many microfilariae was diluted with ten times its volume of a 2 per cent solution of saponin in normal saline and centrifuged at 2 000 r.p.m. for 10 minutes. The sediment was again washed with the saponin solution several times with normal saline and finally with distilled water and dried in a vacuum. It contained microfilariae and leucocytes but no red cells. Normal blood was similarly treated as a control.

For the precipitin test a 1 per cent suspension of the powdered dry antigen in normal saline was used at dilutions of from 1/100 to 1/25 600. This was placed above undiluted serum in small tubes for a ring test which was read after 1 hour at room temperature.

The test was applied in 26 cases with microfilariae in the blood but with no signs or symptoms of the disease; in 14 cases with signs and symptoms but with no microfilariae in the blood; and in 10 normal controls. The result was positive in two of the 26 patients at dilutions of 1/1 600 and 1/800 respectively, and in three of the 14 patients at dilutions of 1/3 200 (2) and 1/1 600. It was negative in all the controls. An extract of dried leucocytes was tested in the group of 14 sera and in the 10 controls with negative results in all.

The authors make no comment on the results. *J F Corson*

MAZZOTTI L. Examen de 400 diafragmas humanos en la ciudad de Mexico para investigar triquinosis. Consideraciones sobre el examen de 1 000 diafragmas. [Examination of 400 Human Diaphragms in the City of Mexico for the Study of Trichiniasis, with a Discussion of the Results of the Examination of 1,000 Diaphragms.] *Rev Inst Salubridad y Enfermedades Trop Mexico* 1944 June v 6 No 2 157-61. English summary.

The author examined 400 human diaphragms in the City of Mexico by compression of 10 gm. of muscle and digestion of samples negative to compression. By compression 46 (11.5 per cent.) were positive while 354 were negative both by compression and digestion. Negative results obtained by digestion were due the author thinks largely to digestion of calcified cysts [cf MAZZOTTI and PASTRANA this *Bulletin* 1944 v 41 958]. Previously MAZZOTTI and CHAVIRA [ibid 1944 v 41 861] examined 600 diaphragms in the City of Mexico. Of these 527 were examined by digestion of only 2 gm. of muscle and 19 were positive. By digestion of the remainder of the muscle sample two more were positive. Thus 21 out of 527 diaphragms were positive (4 per cent.). The remaining 73 were examined by compression of 10 gm. muscle supplemented by digestion of samples negative to compression. Of the 73 9 (12.3 per cent.) were positive.

[March 1945]

Thus 473 were examined by compression of 10 gm. of muscle (i.e. 73 of the 1943 series and 400 of the present series). Of these 473 samples 57 were positive by compression and none by digestion, making a total of 12 per cent. positive. Of the total of 1 000 diaphragms (400 of the present series and 600 examined by MAZZOTTI and CHAVIRA (*loc cit*)) 78 were positive (19 per cent. of 2 gm muscle and 57 by examination of 10 gm. muscle) the total percentage of positives being thus 7.8. PERRIN (*Ciencia* 1939 v 3 108-114) examined 200 diaphragms in the City of Mexico by compression only and found 25 (12.5 per cent.) to be positive. Adding Perrin's 200 to the 600 of Mazzotti and Chavira and the 400 recorded in this paper the percentage incidence in the City of Mexico works out at 8.5 per cent. He suggests that the 12 per cent. of because 527 were examined by compression of only 2 gm. of muscle a method which the author considers to be defective. He suggests that the 12 per cent. of positives obtained by compression of 10 gm. of muscle is nearer the true figure of a larger portion. The author concludes that the compression of a small portion and digestion will probably reveal infestations which are missed by compression. Digestion is costly and laborious and further work will show whether it should be used for routine work or only in special cases.

G. LaPage

SPRU

COOK, A. B. A Vitamin B Deficiency Syndrome allied to Sprue. *Indian Med. Gaz* 1944 Sept v 79 No 9 429-37 (13 refs)

Every practitioner in Gujarat is familiar with the triad of diarrhoea, glossitis and anaemia. Hardly a day passes without a typical case being seen. There is some doubt whether this is classical sprue or the expression of some vitamin B deficiency allied to it.

The salient features are — Copious watery diarrhoea the stools being yellow or white. Glossitis. The tongue is inflamed, usually clean with red spots or glazed in appearance. Glossitis may precede the diarrhoea, may accompany or follow it. Pigmentation of the skin is reflected in black knuckles and sallowness of the face.

The critical difference between this and classical sprue lies in the nature of the motions — the porridge-like bulky frothy stool of sprue is seldom seen. Undoubtedly this must be regarded as a member of the sprue syndrome and the well-appreciated deficiency in the diet of Indians of the vitamin B complex the reaction of these patients to its administration lead to the conclusion that the syndrome is due to B deficiency. Another observation which lends force to this argument is that several cases may be met within one family. The disease, then is the most serious nutritional defect in Gujarat. Dyspepsia is a prominent feature. The patient complains that he is unable to eat. Prominent are gurgling in the abdomen and urgent desire to defecate after food. Constitutional effects are loss of weight, especially tingling and burning of mental power and inability to concentrate. There may be loss of knee jerks. Paraesthesiae are frequently complained of especially tingling and burning of legs, soles of feet and palms of hands. The skin may be dry and scaly. Fever of low degree may often be observed.

over the forearms and legs and signs of loss of weight evident. In advanced cases oedema is due to hypoproteinaemia. Low blood pressure readings are constant.

It is realized that for every fully-developed case there may be several which exhibit but part of the syndrome.

The anaemia is typical of the megalocytic type and the colour index 0.9 or higher. There may be absolute achlorhydria or hypochlorhydria. Only two showed a practically normal curve. The glucose tolerance curve was of the flattened type.

The typical appearance of the rectal mucosa by sigmoidoscope is that of a pale, thin-walled mucous membrane but in acute relapse it may be reddened and oedematous. In this syndrome there may be no increase of fats in the faeces.

The syndrome is definitely relieved by therapy supplying the vitamin B complex by the mouth in the form of nicotinic acid or riboflavin or in extreme cases by injection of the former which definitely controls vomiting and has an effect on the glossitis.

Thirteen cases are quoted in which this syndrome was precipitated by pregnancy but the general explanation put forward is that the mechanism of this syndrome is implanted on dysentery. A conditioned deficiency of vitamin B due to dietetic restriction or defective absorption leads to jejuno-ileal insufficiency and it is possible to trace the change over from a colitis to disorder of the small intestine. Acute relapses may mimic dysentery.

P. Manson Bakr

CHAUDHURI R. N. & RAI CHAUDHURI M. N. Para-sprue. A Study of 22 Cases. *Indian Med Gaz* 1944 Sept v. 79 No 9 404-8 1 chart [10 refs.]

Chronic diarrhoea with sore mouth and anaemia suggestive of sprue has long been recognized in Bengal as a chronic deficiency disease. For this condition the term para sprue has been employed.

The subjects of this study were 22 patients comprising 6 Europeans, 4 Anglo-Indians and 12 Indians—in all 16 males and 6 females.

The duration of the illness extended for six months to two years—with an average of one year. A previous history of dysentery or colitis was obtained in 14 cases.

The onset was insidious, the number of stools varying from 2 to 4 in 10, 5 to 10 in a similar number and more than 10 in 2. In eight the diarrhoea was watery, pale and frothy sometimes with mucus or mucus and occasional blood in the remaining six.

All except one had sore tongue. Other symptoms included loss of weight, flatulency in eleven, anorexia in nine, low fever in four, and nausea in two. Twelve were emaciated, six had oedema of legs, the abdomen was soft, flabby and distended. The right iliac fossa was tender in four and the colon palpably thickened in six. Blood examination showed four markedly anaemic (haemoglobin 6.6 gm. or less), seven moderately anaemic and eight slightly so. The anaemia was macrocytic and hyperchromic and leucopenia was present in a third of the cases. The sedimentation rate was variable, being 20 mm or less in nine out of 20 cases. By keeping each patient on a standard diet containing no more than 100 gm. of fat for three consecutive days, the total fat was 20 to 25 per cent of the weight of dried faeces in nine, 26 to 30 per cent in seven, 31 to 33 per cent in five and 42 per cent in one only. In most cases it was adequately split.

The glucose curve showed that, in half glucose absorption was poor but power to use it remained unaffected.

Treatment consisted of a diet as liberal as possible according to the patient's condition: those with much diarrhoea and anorexia had liquids, often supplemented by intravenous glucose.

In the six who received no medicine the stools became formed soon after the diet was changed from low caloric fluids to a well-balanced diet along with parenteral liver extract. Five had sulphaguanidine in the customary doses and this appeared most efficacious in stopping diarrhoea. Liver (Lilly's T.C.F.) in crude extract was injected in all cases.

For achlorhydric patients dilute hydrochloric acid and glycerol of pepsin were prescribed: two had marmite and one nicotinic acid and riboflavin.

Marked improvement resulted in all but one who died. The weight increased by 25 to 30 lb in two by 10 to 20 lb in five.

Para-sprue constitutes a distinct disease and occurs not only in poor Indians but also in well-to-do Europeans and Anglo-Indians. A history of previous dysentery or colitis is general.

The main distinguishing features from sprue are: the racial distribution, the type of stool and chemical composition, the absence of extreme emaciation and peculiar waxy pallor, and the improvement on parenteral liver extract in the absence of strict dietary regime.

P. Manson-Bahr

HARRISON H. E. TOMPSETT R. R. & BARR D. P. The Serum Potassium in Two Cases of Sprue. *Proc Soc Exper Biol & Med* 1943 Dec v 54 No 3 314-15

"Two cases of sprue are reported in which the values of the serum potassium were found to be at low levels: 1.1 meq L. to 1.6 meq L. [milli-equivalents per litre] before the institution of treatment.

DE FIGUEIREDO F. V. O primeiro caso de sprue tropical no Brasil. [The First Case of Tropical Sprue in Brazil. *Hospital Rio de Janeiro*, 1943 July v 24 No. 1 121-38 6 figs. 41 refs]

A continuation of the paper abstracted in this *Bulletin* 1943 v 40 261 and dealing with diagnosis.

WILDER R. M. Jr. The Nontropical Sprue Syndrome. Report of Four Cases and of a Case in which Intestinal Insufficiency was corrected by Operation. *Proc Staff Meetings Mayo Clinic* 1944 June 14 19 No 12 297-302.

HAEMATOLOGY

ARONAD \ Macrocytic Anaemia. The Unknown Haemopoietic Factor in Whole Liver and Yeast. *Indian Med Gaz.* 1944 Sept. v 79 No. 9 414-18. (13 refs)

VAMIER in 1938 recognized that macrocytic anaemias in the tropics including those of pregnancy could be grouped (on therapeutic grounds) into (a) curable with refined liver extracts (anahaemin) or marmite (b) curable with crude liver

extracts or marmite and (c) curable with campolon. It is now claimed that a fourth group exists which resists campolon but yields to whole liver or yeast. However this anti-anaemic substance has not yet been identified. In such refractory cases clinical evidence suggests that deficiency of nicotinic acid exists alternatively whole liver or yeast may be employed in treatment.

Five illustrative cases are cited. The anaemia resisted parenteral liver during the second and fourth attack in cases 1, 2 and 4 in the late stages of the first attack in cases 3 and 5 when signs indicating secondary pellagra could be detected. These and other facts suggested that resistance to parenteral liver developed only when nicotinic acid deficiency reached a certain degree of intensity.

The author concludes that nicotinamide depletion in the body can reach a stage when the supply of known anti-anaemia factors in the form of parenteral liver extract and marmite cannot produce blood regeneration in such cases exhibition of nicotinic acid alone or in combination with other routine treatments may act almost dramatically in bringing the blood picture to normal.

It is further suggested that nicotinic acid is the factor that acts when cases refractory to parenteral liver rapidly yield to whole liver or yeast.

P. Manson Balr

VALENTINE W. N. & NEEL J. V. Hematologic and Genetic Study of the Transmission of Thalassaemia (Cooley's Anemia, Mediterranean Anemia). *Arch Intern Med* 1944 Sept. v. 74 No. 3 185-96 5 figs. [22 refs.]

This is a study of three cases of Cooley's anaemia or thalassaemia and of one case of a milder but similar form of anaemia the latter was first described by WINTROBE *et al* (*J Amer Med Ass* 1940 v. 114 1530) and later by DAMESHEK (*Amer J Med Sci* 1940 v. 200 445) as 'target cell anaemia' and by STRAUSS *et al* (*Amer J Med Sci* 1941 v. 201 30) as 'familial microcytic anaemia'. The authors have collected haematological and genetic data from 34 members of the four families studied.

They state that it must be regarded as established that a mild familial anaemia qualitatively similar to thalassaemia may be present in both the parents and many of the siblings of patients who have thalassaemia. Three chief theories have been advanced: (1) thalassaemia is produced when the genetic causal factor is homozygous the mild anaemia being produced when it is heterozygous i.e. the factor is either an incomplete recessive or a semi-dominant factor. (2) both conditions are due to a dominant factor which is variously expressed i.e. one person heterozygous for the factor may develop extreme thalassaemia while another person may only have mild anaemia. (3) thalassaemia is caused by the simultaneous presence of two non-allelomorphic dominant factors one being inherited from each parent. The authors have examined the data of other workers statistically and discuss the results. Pending the collection of further data they think that the most satisfactory hypothesis is that of an incompletely recessive factor being the cause.

Certain persons are carriers of the disease the criteria for diagnosis are discussed and the pitfalls that may lead to erroneous diagnosis are mentioned. The authors state that thalassaemia is the first inherited condition of any medical importance in which it seems possible to detect carriers with a high degree of accuracy.

With regard to the terminology of the two conditions the authors suggest the terms 'thalassaemia major' and 'thalassaemia minor' the latter must

brought to hospital on account of obstruction of the left nostril by a tumour which had been growing steadily since it had first been noticed, eight months before. It was now the size of a large filbert—it was removed and the base cauterized. It showed the characteristic histological features of *Rhinosporioidism*. The remainder of the paper is taken up with an account of the literature of the subject since SEEBER's first description in 1896 to the present, with notes of cases reported and a description of the pathological histology taken (as is frankly acknowledged by the authors from ASHWORTH's article in the Transactions of the Royal Society of Edinburgh [this *Bulletin* 1923 v 20 451]. There are four microphotographs and a reproduction of Ashworth's plate. The article is well documented.

H. Harold Scott.

HEAT STROKE AND ALLIED CONDITIONS.

PITTS G. C., JOHNSON R. E. & CONSOLAZIO F. C. with the technical assistance of J. POTLIN, A. RAZOYK & J. STACHELEK. Work in the Heat as affected by Intake of Water, Salt and Glucose. *Amer J Physiol* 1944 Sept. 1 v 142, No 2, 253-8 1 fig. [18 refs]

This paper deals with the performance of work by fully acclimatized men working in the heat intermittently. Therefore in the authors' words "the results are applicable to steel-workers, miners and soldiers in the desert, all of whom usually do a day's work in the heat and spend the rest of the time in cooler surroundings."

The subjects marched uphill on a treadmill for one to six hours a day either in dry heat (100°F 90 per cent. relative humidity) or in wet heat (90-95°F 83 per cent. relative humidity). In all experiments measurements were made at intervals of pulse rate, rectal temperature and rate of sweating. In some cases oxygen uptake, plasma protein, and plasma chloride concentration were also measured.

The first variable investigated was water intake. When no water at all was given pulse rate and rectal temperature rose steadily and never reached a plateau; the rate of sweating steadily declined, mechanical efficiency decreased as shown by an increase in the rate of oxygen consumption for a given amount of work, plasma protein and plasma chloride concentrations rose. The effects were essentially the same in both moist and dry conditions; the moist heat evidently imposed the greater strain because the rate of sweating was about 50 per cent. greater than in the dry heat. In the most extreme moist heat very few subjects were able to complete two hours' work without water.

When water was given all these ill-effects were avoided. Rises in pulse-rate and rectal temperature were moderate and not progressively increasing; there was no decline in rate of sweating or in mechanical efficiency, and no rise in plasma chloride or protein. Most important of all, the subjects were able to work for a full period of six hours. It should be emphasized that in order to obtain the best performance water must be given in amounts equal to the volume of sweat lost. When it is given *ad libitum* performance is not so good. This is because, as first pointed out by DILL, ADOLPH and co-workers, at high rates of sweating thirst is apparently not an adequate stimulus for the immediate replacement of the fluid lost. The amount of water drunk in the day during the period of working and sweating, is usually about two-thirds of the amount of sweat lost; the deficit is made up at night when food is taken.

In other experiments 0.2 per cent NaCl or glucose (25 gm per hour) dissolved in water was given in amounts equal to the amounts of sweat lost. In neither case was performance better than when water alone was given. Nor was any advantage found from giving yeast 200 mgm of ascorbic acid 20 mgm of thiamin or 20 mgm. of riboflavin whether singly or together either during work or the day before.

[This work is very relevant to a question that arises from time to time—namely whether men can be trained to do without water for hours on end in a hot climate e.g. to go all day without drinking. These experiments show that in severe conditions if performance is to be maintained water must be taken from hour to hour as fast as it is lost. Provided the overall intake of salt food and vitamins is adequate water is all that is necessary to prevent rapid deterioration—which must therefore be solely due to water loss. Since at high temperatures the rate of sweating cannot be reduced without risking other dangers it is difficult to see how any acclimatization is possible.]

Even if the body could accumulate reserve stores of water when the rate of sweating was a litre or more per hour these stores would be rapidly exhausted. In the face of this and other recent physiological evidence it would seem that the old tradition of mountaineers and athletes that it is a bad thing to drink on the march is probably founded on psychological grounds and is certainly not applicable to work in the tropics.] *J Waterlow*

PETERS J P Water Exchange *Physiol Rev* 1944 Oct v 24 No 4
491-531 [458 refs.]

The main subjects treated in this review are as follows —

(1) Membrane equilibria and transfers of water within the body. This includes methods of measurement of blood volume extracellular fluid volume and total body water with some discussion of the results obtained by different workers.

(2) Exchanges of water with the environment. Under this heading come thirst water exchanges in the alimentary canal loss of water by sweating and insensible perspiration and metabolic measurements of water balance.

(3) Regulation of the body fluids by the kidneys.

(4) The action of endocrine glands. This section is devoted mainly to diabetes insipidus and adrenal cortical insufficiency.

(5) The effects of diet water and salts—their deprivation and excess.

J Waterlow

MASON Eleanor D Daily Measurements of Basal Metabolism, Body Temperature and Pulse Rate during a Journey to the Tropics. *Indian J Med Res* 1944 May v 32 No 1 27-30 1 graph

Daily measurements of basal metabolic rate pulse rate and temperature were made by the author on herself in the course of a six weeks voyage from San Francisco to Madras. The transition from temperate to tropical conditions was abrupt. For the first two days after this both basal metabolism and mouth temperature rose slightly. From the third day the metabolic rate began to fall and after a week in the tropics was 10 per cent lower than the average rate for that subject in a temperate climate. During the second week it fell slightly more. The mouth temperature regained its original level.

These findings confirm previous work by the same author in which she showed that some but not all people had a basal metabolic rate about 10 per cent lower in the tropics than in a cool country. They suggest that a fall in heat

BLAGOVESHCHENSKI, D. I. BRZOKTOVA, N. G. & MONCHADSKI, A. S. [Activity in Mosquito Attacks under Natural Conditions and its Diurnal Periodicity] *Zool Zh. Moscow* 1943, v 22, No. 3 138-53, 3 graphs [In Russian. English summary]

An abstract of this paper is published in *Rev. Applied Entom.* Ser. B, 1944 Nov v 32 Pt 11 214

HOPKINS G. H. E. Notes on Myiasis especially in Uganda. *East African Med J* 1944 Sept v 21 No 9 258-65 [16 refs.]

The author records a number of cases of human myiasis from Uganda with particulars of the species of fly responsible

The classification of myiasis (which is not solely a matter either of entomology or of pathology) has been unsatisfactory. The author propounds a system based mainly on the organ attacked (e.g. gastro-intestinal myiasis) but including the new term lesionary myiasis for infestations occurring partly at least in diseased tissues on or near the surface of any region of the body. He points out that there are two subdivisions of this in the one the larvae are limited entirely to diseased or damaged tissues in the other they extend also into those which are healthy

Among the Uganda records it is interesting to see a case apparently the first ever recorded of infestation of man by maggots of *Chrysomya inclinata* they occurred in a burn. *Chrysomya bezziana* which so frequently causes lesionary myiasis of man and animals in India has never been recorded from human beings in Africa though common in domestic animals in some areas three human cases are here recorded

P. 4 Huston

ISOOLA W. & OSMANI J. J. Un nuevo caso de oftalmomiasas conjuntival producida por *Oestrus ovis* L. en el Uruguay. [A Case of Conjunctival Myiasis Due to *Oestrus ovis* in Uruguay] *Arch. Uruguayas de Med. Cirug. y Especialidades* 1944 Sept. v 25 No 3 260-61 1 fig. [12 refs.] English summary

VARGAS L. Nombres y datos nuevos de simuliidos del nuevo mundo. [New World Simuliidae] Reprinted from *Rev. Soc. Mexicana de Historia Natural* 1943 Dec 4 Nos 3-4 135-46 7 figs on 9 pls. [37 refs.] English summary

KHOKILOVA-BUYAKOVA O. F. [On the Reaction of Phlebotomus to Different Stimuli in relation to its Distribution in Houses.] *Zool Zh. Moscow* 1943 v 22, No 2 67-72 [In Russian. English summary] Summary taken from *Rev. Applied Entom.* Ser. B 1944 Nov v 32, Pt 11 213-14]

Laboratory experiments similar to those of Polezhaev with mosquitoes were carried out in the summer of 1939 in Sebastopol to ascertain the effect of light on *Phlebotomus papatasi* Scop. When sandflies in a transparent cage were disturbed they all flew immediately towards the wall that was illuminated (796 lux) but soon settled on other walls as well though about 40 per cent. were still on the illuminated wall after 10 minutes. If sandflies were disturbed when the cage was between a window and an electric lamp producing illuminations of 190 and 145 lux, respectively on the walls they always flew first towards the window but again soon distributed themselves evenly over all the walls. The mutual flight towards the window occurred even if the illumination of the wall

nearest it was reduced to 48 lux and that of the wall nearest to the electric light was increased to 500 lux which showed that sandflies like mosquitoes are more attracted by a large illuminated surface than by a small though brighter light.

In another series of experiments fully fed females or hungry ones that had completed digestion were placed in a plywood box painted black on the inside in which the front wall was replaced by a translucent screen through which light of various intensities was admitted. In some cases the screen consisted of adhesive paper so that sandflies alighting on it were caught. The sandflies were disturbed in darkness five minutes before the box was illuminated and then exposed to light for five minutes. Most of them settled on the wall opposite the translucent screen which was lighter than the other walls but the fed females did not react in this way unless the intensity of light on this wall was at least 27 lux whereas the hungry ones did so when it was only 5 lux. It is thought probable that this back wall functioned as a second light screen and that the sandflies alighted more readily on it than on the smoother surface of the screen that admitted the light. The numbers of the sandflies caught on the adhesive paper were little greater than in a control experiment in which the box was not illuminated but were greater in hungry than in fed females showing that positive phototaxis in the reaction of escape is more sharply defined in the former.

Observations in inhabited houses showed that differences in light intensity do not affect the selection by sandflies of places in which to rest during the day provided that the intensity is not greater than 336 lux. From these observations and others in insectaries it is concluded that sandflies are negatively geotactic and to a less extent positively thigmotactic as they usually settle near the ceiling and tend to congregate close together in corners and to hide in cracks. Sandflies entering inhabited rooms through open windows were caught on an adhesive screen fixed in the centre of each window and also on strips of adhesive paper round the edges of the frame showing that some fly in directly and other alight when entering. Twice as many males were caught as females and twice as many hungry females as engorged ones.

VANDERPLANK F L. Apparent Densities of certain African Blood Sucking Insects (Diptera). Reprinted from *Proc Roy Entom Soc of London Ser A*. 1944 June 22, v 19 Pts. 4-6 68-72

FEDER I A. Tick Bite Pyrexia. *J Amer Med Ass* 1944 Sept 30 v 128 No 5 293-4

During military manoeuvres in Tennessee USA in May and June 1943 some patients were admitted to hospital with fever with associated headache and anorexia and occasionally vomiting and abdominal pain. Ticks were found attached to the skin and their removal was followed by complete recovery within 12 to 36 hours. No cause of the illness could be found and the author presumes that it was due to a toxin or venom secreted by the female tick [the species of tick is not mentioned]

EWING H E. Note on Taxonomy of Type Species of the Mite Genus *Trombicula* Berlese. *U.S. Nav Med Bull* 1944 Oct. v 43 No 4 837-9 1 fig
J F Corson

BULL. INST. HYG. MAROC. 1943 v 3 194-7 Rapport sur l'activité du Service central de l'hygiène scolaire en 1943. [Report of the School Medical Service of Morocco for 1943.]

LAWES, C. H. W. & KROX-COREY B. T. Papuan Interiors. *Med. J. Australia* 1944 Sept. 30 v 2, No. 14 354-6 8 figs

BOOK REVIEW

WAR DEPARTMENT Washington. Technical Manual. Emergency Food Plants and Poisonous Plants of the Islands of the Pacific. April 15 1943 (T&I 10-420) [MERRILL, E. D.] pp. v + 149 113 figs 1943. Washington Supt. of Documents, U.S. Govt. Printing Office.

This pocket-sized booklet contains short descriptions and drawings of over a hundred plants and trees which grow in the South Pacific islands the Malay Peninsula, the Philippines, Indo-China, Thailand, Burma and eastern India. It is intended to help the soldier sailor or airman who has become isolated from his unit and has to live on the country. Familiar vegetables and fruits are not included. The botanical and common names as well as many local native names are given. The greater part of the book refers to food plants but there is a section on poisonous plants and a few pages deal with plants used for stupefying fish. The value of local native knowledge is emphasized and native help should be fully used. With such assistance this book should be very useful in enabling the stranger to become familiar with many valuable food plants and some harmful ones.

J. F. CORSON

BUREAU OF HYGIENE AND TROPICAL DISEASES

TROPICAL DISEASES
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[No 4

SUMMARY OF RECENT ABSTRACTS *

III MALARIA.

[Continued from p 165]

Treatment.

General—In a circular letter from the Office of the Surgeon General of the U.S. Army (p 96) on the suppression and treatment of malaria the routine use of pamaquin (plasmoquine) is not advised. Mepacrine does not affect the flight capacity of aviators and is the drug of choice for suppressive therapy in doses of 0.6 gm. or 0.4 gm. each week. For treatment of an attack mepacrine may be given in 0.2 gm. doses every 6 hours for five doses followed by 0.1 gm. thrice daily for six days. For quinine the suppressive dose is 10 grains daily the curative dose 15 grains thrice daily for two days followed by 10 grains thrice daily for five days. [In hyperendemic areas it is probable that suppression requires 0.6 or 0.7 gm. mepacrine weekly and that 10 grains of quinine each day is ineffective.]

NELSON JONES (p 537) has compared three standard courses of treatment of subtertian malaria in the Gold Coast. He found that quinine 30 grains daily for seven days followed by quinine 20 grains daily for seven days was far preferable to a quinine-plasmoquine or a quinine-mepacrine-plasmoquine course in that complete recovery was quicker and progressive ill-health less common. There is no evidence that plasmoquine reduces the relapse rate of *P. falciparum* infections and the author would prefer to abandon the use of this drug.

RAPER *et al* (p 647) have investigated the effect of treatment lasting only three days on malaria in immune and non immune Africans. An immune African for the purpose of this experiment was one who was brought up in a district in which the transmission season exceeded six months in the year. Three different courses of treatment were compared one with quinine one with mepacrine and one with both. It is concluded that immune Africans with malaria need not be admitted to hospital but that for non-immunes admission is desirable. All three courses were satisfactory the combined course being the best.

*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1944 v 41. References to the abstracts are given under the names of the authors quoted and the page on which they appeared.

CURD (p. 101) has compiled, from the extensive literature available a table of the activity of a large number of drugs in malaria of man, monkeys and birds.

KOWLSCHUTTER *et al* (p. 454) have estimated the lethal doses of pamaquin, certuna, mepacrine and quinine for fowls and describe the pathological appearances produced by these doses. They emphasize, however, that the symptoms produced in birds by the toxic action of these drugs are different from those produced in man.

Quinine—LOWE (p. 997) makes the point that unnecessary delay in instituting treatment for malaria is criminal. He gives higher initial doses of quinine in *P. falciparum* than in *P. vivax* infections and prefers oral administration if possible. If quinine must be injected, the intravenous rather than the intramuscular route should be adopted.

From experiments in birds, BECKMAN and SMITH (p. 545) conclude that treatment with quinine given every two hours is more effective than that given less frequently but in the same total dosage. This would indicate that continuous administration in man might justifiably be tried.

McGUIRE (p. 539) has found that quinine sulphate solution can be used for intramuscular injection. It is no more prone than the dihydrochloride solution to cause abscess. [But, as the salt is dissolved in an acid solution one would expect more muscle necrosis than with a solution more nearly neutral.]

In a discussion of malignant and atypical malaria, KREEDLER (p. 450) advocates treatment with quinine (intravenously or intramuscularly) in the early stages, followed by mepacrine. There is never any indication for intravenous mepacrine since only small doses are advisable by this route but if necessary it can be given intramuscularly.

YOUNG and MACADAM (p. 724) condemn large intravenous doses of quinine as a first treatment of cerebral malaria, preferring an immediate intramuscular injection followed, 4-6 hours later by a small intravenous injection of 3-6 grains. This may be repeated to a total of three injections.

ROGAN (p. 921) treats cerebral malaria by intravenous quinine given slowly and repeats the injections (up to a total dosage of 30 grains in 24 hours) until recovery from coma takes place. GILBERT (p. 538) has successfully used intravenous pentothal sodium to control patients with cerebral malaria of violent maniacal type. Intravenous quinine was given while the patients were the influence of this narcosis.

KELSEY *et al* (p. 11) have determined the distribution of quinine in the tissues of the fowl. There is great variation in the blood concentration after oral administration, and when repeated doses are given, most of the drug is detoxified each day. Details are given in the original abstract. KELSEY *et al* (p. 923) show that when quinine is incubated with certain animal tissues it is converted into substances which no longer have the solubility or fluorescent characteristics of quinine. BECKOX, KELSEY and OLIPHANT (p. 260) have shown that quinine is present in the foetus of the pregnant rabbit after it has been given to the mother—that the placenta has some power to impede the passage of quinine—that the power of the liver of the pregnant rabbit to destroy quinine is not so great as that of the non-pregnant rabbit. Certain animal tissues destroy quinine *in vitro* and oxygen is required in this process. There is great variation in the activity of the different tissues in this respect. The agent responsible for this destruction is termed quinine oxidase and the loss of liver activity in the destruction of quinine during pregnancy appears to be due to lack of this enzyme rather than to some inhibitory mechanism.

KROGH and SHAW (p. 1003) have sought to elucidate the action of quinine in malaria, and as a result of their experiments they conclude that there is a

physiological antagonism between quinine and calcium and that quinine interferes with growth and reproduction of the malaria parasite by reducing the amount of calcium available in red cells

JOHNSON and SCHNEVER (p 923) have investigated the quinine inhibition of bacterial luminescence with a view to throwing some light on the action of quinine on malaria parasites The paper should be studied in original

HOWIE and MURRAY LYON (p 185) have studied the Tanret reaction in relation to the ingestion of quinine In 100 patients undergoing quinine treatment seven failed to give a positive reaction and five were positive at irregular intervals These men responded poorly to the treatment, but reacted well to injection of quinine In 53 healthy persons the reaction became strongly positive within five hours of taking quinine though there was considerable individual variation and it was negative again after 24 hours It is recommended that quinine dosage should be regulated for each person by the results of the Tanret test

BARANGER and THOMAS (p 103) have shown that the total alkaloids of *Cinchona* from West Africa are as effective as quinine against *P. falciparum* in canaries but that the total alkaloids from which quinine has been extracted have poor therapeutic effect JOHANNESSEN (p 727) describes Prochinin a mixture of cinchonine cinchonidine and quinidine which has been used successfully by the Germans in malaria GALPERIN (p 825) discusses the antimalarial action of quinoline compounds

Alkaloids from the bark of *Alstonia* (widely distributed in Australia) though resembling quinine in many respects were found by KEOGH and SHAW (p 335) to have little antimalarial effect in animals

Mepacrine and Pamaquin.—HAWKING (p 1005) has examined the local effects of mepacrine dihydrochloride mepacrine methanesulphonate and quinine dihydrochloride when injected intramuscularly The damage caused to muscle by the two salts of mepacrine is far from negligible though probably less extensive than that caused by quinine The oral route is therefore to be preferred to intramuscular injection if this is possible Mepacrine should not be given subcutaneously or intravenously

KIRZON (p 281) treats his cases of severe malaria by injection of mepacrine intramuscularly the dose being 0.3 gm. in 10–12 cc. water The usual course is one injection each day for 3–5 days Blood transfusion is also beneficial FERNANDEZ MARINA (p 1004) gives details of a course of treatment in which mepacrine is given intravenously as well as by mouth The method is safe [but compare HAWKING above]

EPSTEIN (p 451) has adopted an initial large dose of mepacrine (0.5–0.6 gm. on the first day) in his treatment of benign and malignant tertian malaria This produces earlier termination of fever than 0.3 gm. on the first day In each case the drug is continued in daily doses of 0.3 gm.

KONJ and YAKOVLEVA (p 922) have adopted a prolonged course of mepacrine and pamaquin treatment in an area of central Russia in which *P. vivax* is the common parasite for the prevention of relapse and show that this has been more successful than a shorter course Mepacrine is given in daily doses of 0.2 gm. for periods of 3–5 days alternating with 10-day intervals throughout the period when relapses occur (April–June) The later courses include pamaquin in 0.04 gm. doses

The toxicity of mepacrine has been investigated by several workers —

KAHLER (p 451) describes two cases of unusual reactions to mepacrine in comment HAWKING points out that such happenings are rare WRIGHT and LILLIE (p 99) give an account of the toxic effects produced by heavy doses of mepacrine and sulphadiazine but in comment HAWKING remarks that these

In a well-controlled investigation LONGGILL *et al.* (p. 186) showed that American mepacrine (atabrine) is no more toxic than the German product, and that, in the usual suppressive doses it does not normally cause important toxic reactions.

WAELESC and VACHMANSOHN (p. 649) postulate that the toxic action of mepacrine may be due to the fact that it inhibits choline esterase the substance which destroys acetyl choline and that the result is similar to stimulation of the vagus.

SCUDI *et al.* (p. 723) show that with doses of one-half the LD50 mepacrine was fatal to a high proportion of rats which had received no food for 12-36 hours especially if their previous diet had been deficient in protein. With this dose there was evidence of severe gastro-intestinal irritation, and inhibition of liver function, increased by fasting.

SCUDI and HAMLIK (p. 723) show that the toxicity of mepacrine for rats can be mitigated by a diet rich in protein and poor in fat. In dogs on normal diet, toxic symptoms were produced by continued high dosage of mepacrine, and an increase in plasma fibrinogen indicating destruction of liver tissue was observed. In lower dosage liver damage could be produced if the animals were on low-protein diet, but controls on high protein were not affected.

REGGIE *et al.* (p. 649) have shown that continuous administration of mepacrine to rats on ordinary diets may affect their growth and condition if in high dosage, and may intensify any ill-effect due to the diet if this is deficient in protein or riboflavin. But on a low-protein, low-choline diet the addition of mepacrine seemed to have a protective effect.

PICK and HUYER (p. 924) have shown, by electrical means that mepacrine has a depressant action on the brain of the cat. In comment HAWKING points out that, in man, mental disturbances due to mepacrine are rare unless large doses are given.

BOCK and OESTERLIK (p. 545) describe their observations on fluorescent substances in relation to a number of parasites. Specifically active substances are absorbed by special parts of the parasites (blepharoplast, etc.) whereas of fluorescent but inactive substances is more general, and the is not produced except in relatively high concentration. Monkeys with malaria were treated with mepacrine which was visible in the under the fluorescence microscope before morphological changes took in them. The authors consider that the action of mepacrine is directly upon the parasites.

BRODIE and UDENFRIEND (p. 453) describe a method of estimating mepacrine in biological fluids and tissues, by which amounts as low as 0.1 μ gm. may be estimated, with an error of less than 5 per cent. A simpler but less accurate method is also described.

AXTEGERS *et al.* (p. 98) have examined the retention and excretion of mepacrine in animals details should be sought in the original abstract. SCUDI and HAMLIK (p. 262) have also investigated the distribution and excretion of mepacrine in experimental animals, but for details the original should be consulted. SCUDI and JELINEK (p. 452) describe the urinary excretion products of mepacrine the paper is technical and should be consulted in original by those interested.

SHISHILAEVA-MATOVA (p. 819) has found that a systematic treatment with mepacrine and pamaquin, both therapeutic and suppressive, was not very effective in eradicating infection on a collective farm in a hyperendemic area of Russia, and concludes that for effective control where the vector mosquito population is high, drug treatment should be reinforced by anti-larval measures.

MANSON BAIER (p 1003) does not think that pamaquin should be given in the average case of subtertian malaria and refers to the need to give intravenous quinine slowly in cerebral malaria

MANN (p 100) reports a case in which haemoglobinuria occurred after the patient had been treated for malaria with quinine mepacrine and pamaquin (plasmoquine) The author attributes this to the plasmoquine which apparently has two toxic effects—the production of haemagglutinins which are not specific to the patient's red cells and of a haemolysin and a toxin with direct action on the renal tubules

Other Drugs—JOHNSON (p 100) has treated a few patients inoculated with *P. malariae* with sulphadiazine in daily doses of 4 gm or less to a total dosage of 24–48 gm The results were satisfactory but three of the 13 patients had relapses which were controlled by second courses of sulphadiazine

LOWE (p 825) shows that neocarsphenamine and mapharside have some therapeutic action against *P. vivax* but not against *P. falciparum* or *P. malariae*

Suppressive Treatment

PARROT *et al* (p 539) have carried out experiments on suppressive drug treatments in the native population of highly malarious places in Algeria, where *A. maculipennis labranchiae* is the vector Under the conditions of the experiment [in which no doubt the state of immunity of the people had its importance] it was found that administration of 0.2 gm mepacrine twice each week was as effective as daily administration (except on Sundays) of 0.4 gm quinine. Both drugs diminished the reservoirs of *P. vivax* and *P. malariae* but neither completely suppressed *P. falciparum* during the season of heavy transmission. There were no toxic results from mepacrine except that immediate vomiting was often provoked in infants Suppressive treatment cannot replace other anti-malarial measures

LEVENSON *et al* (p 10) report on a campaign of mass chemoprophylaxis with mepacrine which was apparently successful in reducing greatly the incidence of malaria in the region of Archangel. The dosage was 0.2 or 0.3 gm daily for periods of 2–5 days continued at intervals of 10 days through the spring and summer In comment BUXTON points out that these authors report *P. vivax* and *P. falciparum* in a region further north than any hitherto recorded in Russia. In particular *P. falciparum* has so far only been known in the centre and south of Russia.

TALBOT (p. 97) in a description of malaria in an outlying military base [presumably in the Far East] where antilarval measures were impossible remarks that he does not advise the use of suppressive medication except in an area of actual combat in an endemic area.

CLARK (p 9) has for 10 years been attempting to control malaria in Panama by the administration of anti-malarial drugs to all persons in whom parasites are found at the monthly surveys. In this way the incidence of malaria may be somewhat reduced, but it has not been possible to eradicate it or to prevent relapse. More recent work, done on the basis of survey every two months has confirmed the previous conclusions. He (p 924) contributes another report on control of malaria in Panama by giving treatment to persons found to be harbouring malaria parasites. The parasite rates in those given mepacrine were rather higher than in those given quinine but for various reasons complete surveys and complete treatment were impossible. The author remarks that general opinion seems to underestimate the importance of relapse in *P. falciparum* infections.

Control

A fourth year's study of the efficacy of spray killing adult mosquitoes (*A. culicifacies*) has confirmed previous findings in South India RUSSELL *et al* (p

456) report that it reduces malaria transmission to a marked degree. Houses animal sheds and buildings were sprayed with a pyrethrum preparation usually at weekly intervals, during the transmission season. Results, estimated by spleen and parasite rates, were very good in comparison with control villages, and it is noted that the villagers appreciate the benefits. The cost per person varied from 3 to 7½ annas.

ANVECKE (p. 457) has experimented with various repellents, and concludes that plain citronella oil still holds first place among those tested, provided that it is applied every three hours, but that a cream containing naphthalene and a concentrated extract of pyrethrum was almost as good.

WILSON and MELVILLE (p. 263) describe the general measures taken to reduce the incidence of malaria in the forces serving in the East African Command. The conditions in the different areas varied from continuous transmission to seasonal transmission of different degrees, and in some places there was no transmission. The anti-malaria organization has usually been brought down, in since it became adequate in size, incidence has usually been brought down, in a few weeks, to less than 100 per cent per annum. Malaria-mindedness in the troops is very important and so is camp siting. Track discipline is emphasized since rain-filled car tracks can produce enormous numbers of *A. gambiae*. The proper use of protective clothing and nets is a matter on which discipline should be strict. Repellents have not been much used and head nets have not been successful in practice. Spray-killing of adult mosquitoes in the quarters and other likely resting places is essential, and is always practicable in military malaria control. Anti-larval measures are now regarded as a routine in almost all circumstances, and malaria can be controlled under apparently most unpromising conditions. Siting of course is largely used, but drainage may often reduce the areas to be used. Suppressive drug treatment has not been used to a great extent. It has not often been necessary. The authors finally stress the importance of applying all anti-malaria measures to the maximum possible extent, and give information which demonstrates the success that may be achieved.

RIBBANS (p. 925) points out that camp siting even in areas where there are no places free from anophelines is a most important anti-malaria measure. One factor is the distance of the camp (of uninfected persons) from the nearest infected human population and the risk is negligible if 5 miles intervene and small at 2 miles. Risk is greater if breeding occurs between the village and the camp. Small infected communities are dangerous in that there are fewer persons for the mosquitoes to attack than in larger centres. If complete removal of the infected community is impossible (as it usually is) partial removal is worse than useless unless it is the children (the richest reservoir) who are removed. In choosing camp sites, higher ground should be given preference.

COVELL (p. 646) has contributed a comprehensive review of the prevention and treatment of malaria in war in the light not only of actual wartime experience but also of the researches carried out in the original.

adequately be summarized, and readers should refer to the original. BUTLER (p. 381) describes malaria control in a South Pacific Island where the only vector was *A. punctulatus melanocephalus* which breeds freely in rain pools, road runs, etc. and in semi-shaded margins of pools and streams. The measures taken were not new but all forms of control were used and emphasis was laid on malaria discipline. Very little use, however, was made of insecticides and repellents. Suppressive treatment with mepracine was useful while control was being organized. No toxic effects were seen from a weekly dosage of 0.4 gm. FREEDORF (p. 729) writes of the danger of large-scale introduction of malaria into the United States by troops who will return from the various theatres of war. Anti-anopheline measures are being undertaken in many States, and

particular attention is to be paid to the environs of general hospitals in which presumably there will be comparatively heavy concentrations of parasite carriers.

DE ANDRADE (p 1007) describes the important part played by Paris green in the eradication of *A. gambiae* from Brazil. The best results were given by a type whose particles were about 2 microns in diameter. There was no case of poisoning of animals or man in spite of the widespread use of Paris green.

MURRAY and K. NUTSON (p 1007) report on the good results obtained by dusting with Paris green from aeroplanes once each week in the summer on the breeding of *A. quadrimaculatus* in the Potomac river. ZUMPT (p 265) gives in some detail his experiences with aircraft as a means of scattering Paris green or oil for the control of anopheline larvae. Details of the amounts, diluents and results should be sought in the original abstract. In general the Paris green experiments were successful but the attempts to use oil were abandoned.

NESTERWODSKAJA and LUBINSKI (p 102) have confirmed the high toxicity of phenothiazine to mosquito larvae especially *Anopheles*. In field trials at 12-13°C. with dosages of 7 and 14 oz. per acre all *Anopheles* larvae had disappeared in 48 hours. Phenothiazine is toxic to fish but is practically harmless to mammals [presumably in the doses likely to be ingested under these conditions. In high doses phenothiazine may be very toxic].

NEWBOLD (p 11) describes a self-clearing drainage outlet from coastal swamps which have a ground level about that of high tide. This has successfully been used in Trinidad and Grenada. Details are given in the original abstract. COCHRANE and NEWBOLD (p 102) have achieved satisfactory results in the prevention of breeding of *A. argyritarsis* in a stream in Grenada by the installation of an automatic flushing siphon. They observe that although this mosquito has never been proved a vector it is strongly suspected.

The deliberate increase in salinity of coastal lagoons in the West Indies is effective in controlling the breeding of *A. albimanus* provided that the salinity reaches 75 per cent of that of sea water. HURLBUT (p 266) shows that increased salinity not only reduces the proportion of females which lay eggs but also the proportion of eggs which hatch out.

In the *Boletín Oficina Sanitaria Panamericana* (p 102) is an account of the anti-malaria campaign in the Republic of Panama where *A. albimanus* is by far the most important vector.

COVELL and SINGH (p 455) give an account of an outbreak of malaria which occurred in Delhi in 1942 as a result of exceptionally heavy rainfall in that year. The previous epidemic had occurred 9 years earlier and the general immunity was consequently low. In general the permanent anti-malarial engineering work already done was effective in limiting the outbreak but there were formed nevertheless extensive sheets of water ideal for the breeding of *A. culicifacies*. The chief emergency measure adopted was the spray killing of adult mosquitoes which seemed to be effective.

ADISUBRAMANIAM and VEDAMANICKAM (p 458) have found that antilarval measures against *A. fluviatilis* may reasonably be limited to breeding places within 1 000 to 1,500 feet of the dwellings they are designed to protect.

CUNNINGHAM VAN SOMEREN (p 1006) writes of the use of elephant grass in protecting the banks of drainage canals against erosion and damage.

RECTOR (p 650) has described the method of blasting ditches in wet or marshy land by the use of dynamite a method which was used successfully in anti malaria work in Palestine some years ago.

A group of Russian workers (RAEVSKY *et al.* p 541) have carried out considerable research on the question of prevention of malaria by interposing between human habitations and mosquito breeding places the cowsheds and other animal houses belonging to the communities. They observe that this

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form of prevention is possible in the Soviet Union because animals are common property and can be fully controlled. Evidence is produced that, by proper placing of the animals, the spleen rate and other signs of infection can be greatly reduced, and that the mosquitoes (races of *A. maculipennis*) are diverted from man to the animals. In some places this form of malaria control is the only one possible, but it is advised that zooprophytaxis should be reinforced by suppressive treatment in hyperendemic areas. The barrier consists of a row of animal houses, not less than 200 metres from the human settlement; they should be 45-50 metres apart, and their doors should be on the leeward side. Between the barrier and the village there should be vegetation. Attraction to mosquitoes is through their sense of smell, and is proportionate to the surface area of the animal. Cows and buffaloes are the most attractive; horses are not so effective as cattle.

Malaria of Monkeys and Birds.

MAIER and COGGESHALL (p. 826) have investigated the immunity conferred on monkeys by infection with *P. knowlesi* which was controlled (so as to prevent death) and maintained as a chronic infection for varying periods of time. The infections were rendered chronic by timely doses of quinine, and were terminated by sulphathiazole. From infections lasting only a few days no immunity was conferred but from those lasting several weeks, or longer, partial immunity persisted after sterilization of the infection for periods up to one year. The duration of the chronic infection influenced the degree of immunity but not, apparently, its duration.

ROY and MUKERJEE (p. 103) have shown that during the severe phases of *P. knowlesi* infection the complement in monkey blood is greatly reduced. STODOL and BOSE (p. 825) report that a butyl-acridine derivative has a powerful action against *P. knowlesi*; this may be comparable with the action of mepracrine (which is an anti-acridine derivative).

RODHAIS (p. 544) has succeeded in passing the quartan-like parasite of chimpanzees (*P. rodhaini*) to man and now takes the view that it probably is *P. malariae*.

BISHOP and GILCHRIST (p. 731) have succeeded in collecting sporozoites of *P. gallinaceum* by allowing infected *Aedes aegypti* to feed through a membrane on hepatized blood. The sporozoites so obtained may be used for chemotherapy, peptic experiments.

DAVEY (p. 365) discusses the phases of development of *P. gallinaceum*. In his view the sporozoites leave the blood to enter the tissues (primary tissue phase) thence they re-enter the blood or tissues (secondary tissue phase) represented by the exo-erythrocytic schizonts. These secondary phase forms are capable of indefinite asexual development, whereas the primary tissue phase is probably common to all malaria parasites, the secondary tissue phase has been described definitely only in *P. gallinaceum* and *P. elongatum* and probably in *P. vivax* and the parasites of the primary phase would act on the sporozoites or the parasites of the primary phase.

ADLER and TCHERNOGOROETZ (pp. 103-368-458) have shown that exo-erythrocytic forms of *P. gallinaceum* can produce merozoites which invade red cells and develop into gametocytes.

HAWKING (p. 732) has successfully cultivated exo-erythrocytic forms of *P. gallinaceum* by means of tissue cultures of spleen, liver, marrow and brain of infected chicks.

ZAIN and WOLF (p. 104) have investigated the influence of X-rays on *P. gallinaceum*.

RUSSELL et al. (p. 104) have studied the spleen volume in fowls infected with *P. gallinaceum*.

SCHENG (p 366) has tested quinine atebirin and plasmoquine against exo-erythrocytic forms of *P. cathemerium* *in vitro* in concentrations much greater than can be attained *in vivo*. The results indicate that exo-erythrocytic forms are very resistant to these drugs.

WOLFSON (p 104) has studied infection of ducks with a strain of *P. cathemerium*. A series of rapid passages has increased the intensity of the infection which may now prove suitable for chemotherapeutic research.

REICHENOW and MUDROW (p 190) have traced in great detail the development of *P. praecox* in birds with special reference to the formation of exo-erythrocytic and erythrocytic parasites and of gametocytes. The exo-erythrocytic forms are derived from those parasites which divide into large merozoites, the erythrocytic forms from cells which produce much smaller merozoites, and the proportion of the latter to the former is quickly increased so that after the fifth cycle no further endothelial development takes place. Gametocytes are produced by the first merozoites which enter red cells so that sexual differentiation has already taken place at that stage.

REDMOND and PRATHER (p 267) have compared the infections produced in pigeons and canaries by *P. relictum* [*P. praecox*]. There was little difference so far as the parasite was concerned.

MANWELL (p 268) has studied infections in ducks with four species *P. circumflexum*, *P. elongatum*, *P. nucleophilum* and *P. relictum matulinum*. The duck is a good host for each of these and may be used for chemotherapeutic studies.

JACOBS (p 458) has shown that an antigen containing saline-insoluble residues of *P. lophurae* injected into ducks conferred a degree of protection against subsequent infection which was increased if staphylococcus toxoid was added to each dose just before administration. It is thought that the useful malarial antigens are of the nature of insoluble baptes.

By experiments on ducks infected with *P. lophurae* and treated with quinine WALETZKY and BROWN (p 188) have been unable to exclude the possibility that a metabolic product of quinine is the therapeutic agent.

HEWITT and RICHARDSON (p 188) have obtained evidence that in ducks infected with *P. lophurae* quinine, mepacrine and pamaquin attack the parasite directly, the mechanism of their action is not clear but there is no evidence that they stimulate phagocytosis or other immune reactions.

BARRETTO (p 732) reports that exo-erythrocytic forms of *P. juxtannucleare* have been found.

PATTON and METCALFE (p 546) have shown that fluorescent dyes can be used satisfactorily for the staining of *Haemoproteus* of quails.

SEELER *et al* (p 651) confirm previous work which indicated that deprivation of biotin was deleterious in bird malaria.

THOMPSON and HUFF (p 827) give an account of a new species of *Plasmodium* from a Mexican lizard, and report that exo-erythrocytic forms of this parasite have been found. They also describe the other plasmodia found in Central American lizards.

MANWELL and EDGETT (p 189) report on the importance of certain factors in the low temperature preservation of malaria parasites. For details the original abstract should be consulted.

Charles Wilcocks

MALARIA.

- i. SABROSKY C. W & USINGER, R. L. Nomenclature of the Human Malaria Parasites. *Science* 1944 Sept. 1 180-82.
- ii. HEMMING F. Generic and Specific Trivial Names of the Tertian and Quartan Malaria Parasites. [Correspondence.] *Nature*. 1944 Dec. 2, 701 Also in *Brit Med J* 1945 Jan. 20 85

i. In their opening remarks the authors of this note quote from STILES (1928) "the nomenclature of the parasites of malaria in man and birds represents one of the most confusing chapters in the entire history of zoological nomenclature. They refer to the article on this subject by CHRISTOPHERS and SEXTON [this *Bulletin* 1939 v 38 390] and concur in the conclusions drawn by these writers. They trace the history of the various names which have been proposed from time to time, beginning with LAVERAN's *Oscillaria* of 1881. They find that regarded as belonging to a single genus, the names of the three common parasites of man should be *Oscillaria vivax* (Grassi and Feletti, 1890) *O. quartana* (Celli and Sanfelice, 1891) and *O. malariae* Laveran 1881. As attempts to introduce these names into medical and zoological literature at this late date would cause the utmost confusion the authors suggest that the International Commission of Zoological Nomenclature legalize (what has already been expressed in Opinion 104 and advocated by CHRISTOPHERS and SEXTON) the existing practice of calling the parasites *Plasmodium vivax* (Grassi and Feletti, 1890) *Plasmodium malariae* (Grassi and Feletti, 1890) and *Plasmodium falciparum* (Welch 1897) [For some reason which does not seem to be in accord with the rules of nomenclature the authors write *Plasmodium malariae* (Feletti and Grassi, 1889 1890) and *Plasmodium falciparum* Welch (1897)].

ii. In the second paper from *Nature* Francis Hemming, Secretary of the International Commission on Zoological Nomenclature, invites in connexion with the above discussion, expressions of opinion from specialists concerned in any aspect of the malaria problem.

C. M. Wenyon

MACFIE, J. W. S. Terminology in Malaria. [Correspondence.] *Brit. Med. J* 1945 Feb 3 163.

In an annotation in the *British Medical Journal* of January 20th 1945 approval was expressed of a suggestion by the Reporting Committee of the Malaria Commission of the Health Organisation of the League of Nations [*Bull. Health Organisation* (League of Nations) 1940 v 9 No. 2 146] this was that the specific names of the different malarial parasites should be used to denote the fevers e.g. *vivax* malaria, *falciparum* malaria, &c. When however the author tried recently to use these terms in the commentary of a medical film, it was found that the name *malariae* malaria was almost impossible to enunciate clearly and caused confusion so the attempt had to be abandoned. The difficulty would be avoided if the fevers were named *vivax* tertian *falciparum* tertian, *ovale*-tertian and *malariae*-quartan, although these names are nearly as clumsy as the old ones [See also CHRISTOPHERS & SEXTON this *Bulletin* 1939 v 38 390 SABROSKY & USINGER above HEMMING above J. NAT. MAL. SOC., this *Bulletin* 1944 v 41 996.]

J. F. Corson.

JACKSON A. V. *Plasmodium ovale* Malaria: a Report of Two Cases contracted in New Guinea. *Med. J. Australia*. 1944 Sept. 9 v 2, No. 11 278-9

"*Plasmodium ovale* parasites were found in the blood of two patients at an Australian general hospital in New Guinea. These patients had not previously been in a malarious area, and so presumably the infections were contracted in

New Guinea. *Plasmodium ovale* which has not hitherto been reported from New Guinea is a rare parasite and infections by it should only be diagnosed after a very careful examination of several thin blood films taken at different stages of the asexual cycle

SAMARASENGHE D S, PLYASENA, A K & RUSTOMJEE K J. *P. tenue* Forms and "Band" Forms of *P. vivax* seen in Ceylon during the Epidemic of 1943. [Abstract] *J Malaria Inst of India*. 1944 June v 5 No 3 397

RIBBANDS C R. The Influence of Rainfall, Tides and Periodic Fluctuations on a Population of *Anopheles melas* Theo *Bull Entom Res* 1944 Nov v 35 Pt 3 271-95 8 figs. [19 refs.]

The author has recently pointed out that *Anopheles gambiae* var *melas* is in fact more than a melanic variety of *A. gambiae* breeding in sea water since it differs from the latter in permanent structural and physiological features [this *Bulletin* 1945 v 42, 3]. No certain way of distinguishing all adult *A. melas* from *A. gambiae* has been found, since only a variable proportion possess the *melas* band on the terminal white band of the palp. As a result of the distinction referred to *A. melas* has now been fully recognized as an important vector of malaria in the coastal regions of West Africa.

The experiments described in this paper were carried out near Freetown in Sierra Leone. A map and brief account of the important climatic and geographical features of the district are given. It included two main breeding areas: a brackish grassy breeding area flooded only at high tide (so that in the season of low rainfall it is mainly dry) and a brackish *Avicennia* mangrove breeding area. In the dry season all the water was saline and would support mainly *A. melas* but in the wet season certain parts of the water were almost fresh and were capable of supporting *A. gambiae*. Since however the percentage of *melas* banded individuals in the population remained more or less constant it was concluded that the population at all times was in fact very largely one of *A. melas*.

Two huts were erected near the grassy breeding area and baited with the same natives throughout the experiments. The mosquitoes were caught by covering the floor of the enclosure with a sheet and spraying out with a pyrethrum spray. The mosquitoes collected on the sheets were counted and the results expressed as an index (number of mosquitoes divided by number of natives per hut). The experiments extended from 10th January to 31st October 1941.

The general conclusions arrived at after detailed statistical treatment of the results were as follows. Seasonal variation. The average size of the adult population was closely determined by rainfall, but peak populations only occurred 20-30 days after the causative rainfall and no response was apparent before the lapse of 10 days. Fluctuations in the rainfall level have the greatest effect on the size of the population. The rate of increase in the population after rainfall was very variable, the maximum being 240 per cent. after one eight-day interval compared with a tenfold increase in a similar period following a high tide in the dry season. Short term fluctuations. There was evidence for the occurrence of peaks in the population of *Anopheles melas* in a cycle of not more than 16 days. Certain of these occurring in the dry season were definitely correlated with the occurrence of a high tide seven to nine days previously, in the wet season this correlation was not apparent. Some peaks could be accounted for by previous rainfall, and still others it is suggested may be due to the effects of intra-specific competition in the larval environment. It appears that heavy rainfall does not reduce the adult population by direct killing action.

From the practical point of view it can be seen that *A. melas* is an all the-year round carrier but the dry season population is only about one-tenth of that of the wet season. Although influenced by tides, the *A. melas* population level was more influenced by rainfall, and sharp increases could follow after a rain storm in any season. In the absence of rain, spring tides were the main cause of the breeding of *A. melas* and methods of preventing access of high tides to breeding areas would affect control provided that the protected area was adequately drained in the wet season.

In the dry season, when there has been no appreciable rainfall for six weeks, temporary anti-larval measures, such as oiling and Paris green are only likely to be useful in the four days following maximum spring tides. At other times weekly oiling, or dusting at four day intervals, is necessary.

W. A. L. David

LEWIS D. J. Observations on *Anopheles gambiae* and other Mosquitoes at Wadi Halfa, Trans. Roy. Soc. Trop. Med. & Hyg. 1944 Dec. v 38, No. 3 215-29 1 map & 2 figs. (23 refs.)

Wadi Halfa, the most northerly town in the Sudan, is situated near the northern end of the navigable reach of the Nile just north of the second cataract. It is an important town on the Nile route since it has an aerodrome and is a terminus for railway and steamer services. The area concerned in this study is a narrow belt on both sides of the river extending from the cataract to Faras, some 58 km. downstream. The mosquito fauna is represented by but eight of the 22 species common to the zoogeographical regions to the north and south. *Anopheles gambiae* is the only one considered in any detail, although short notes are given on each of the other species.

There are various reasons for giving attention to the position of *A. gambiae* in the Wadi Halfa area. firstly in order to control malaria in the town itself secondly if *A. gambiae* can be exterminated in Egypt, it might be possible to confine it to the area south of Wadi Halfa. thirdly it might represent a more serious problem if the level of the Aswan Reservoir is increased above its present height since that would extend the now restricted swampy area due to seepage.

The area is a favourable one for the application of mosquito control measures. Geographically it is isolated from the east and west by the desert. climatically the low rainfall (0.2 mm. per annum) and low humidity of the atmosphere are unfavourable for mosquito breeding and survival, while the prevailing wind is almost always northerly so that insects emerging in the cataract area have less chance of invading Wadi Halfa. Finally communications with the surrounding area do not provide a great danger of reinfestation, since boats from the south do not proceed beyond the cataract and other ships, aircraft and trains are treated with sprays.

The main breeding sites are the pools among the islands of the cataract, the pools on sandy banks in mud streams, and those near the margin of the river. These pools are formed by changes in the water level. Under the prevailing conditions *A. gambiae* would pass from egg to adult in about seven days in summer but might take about one month in winter. Breeding appears to cease between mid-December and mid-April. this is presumably due to the fact that the pools dry up before the larvae complete their development. It appears, in fact, that the species dies out since it is unlikely that adults would survive for four months at the low prevailing humidity. The April source of *A. gambiae* is probably the cataract, since larvae have been found in December and March, and it is likely that they persist throughout the winter.

The control measures applied consist of oiling the application of Paris-green, and draining the larvivorous fish *Gambusia holbrooki* is also very successful.

In order to check the spread of infestation from the cataract it was decided to control a six kilometre stretch of river and adjacent cultivated land extending from the cataract to a point about two kilometres north of Wadi Halfa. The assumption was made that few *A. gambiae* would fly northwards beyond this band and it appears to have been fully justified. south of the band a malaria outbreak occurred and *A. gambiae* were found breeding in untreated pools while all but four of the control untreated pools north of the band remained free from *A. gambiae* for ten months.

W A L. David

MARNEFFE H, RANQUE J & SAUTET J. Quelques points de la biologie de *Anopheles (Myzomyia) gambiae* dans la vallée moyenne du Niger. [Points in the Biology of *A. gambiae* in the Middle Niger Region.] *Bull Soc Path Exot* 1943 July 7 v 36 Nos. 7-8 223-6

The authors have studied the precipitin reaction of the blood in about 250 female *A. gambiae* collected in a variety of environments (indoors and out) in and about Bamako on the Niger. Domestic animals were common in and about the villages. In 55 per cent a positive human reaction was obtained. The only available serum was anti human so that the absence of positive reactions to other mammals is without significance.

In about 150 female *A. gambiae* the maxillary index was fifteen to seventeen.

P A Buxton

SHAPIRO J M, SALITERNIK Z & BELFERMAN S. Malaria Survey of the Dead Sea Area during 1942, including the Description of a Mosquito Flight Test and its Results. *Trans Roy Soc Trop Med & Hyg* 1944 Nov v 38 No 2 95-116 1 map 1 pl. & 1 chart

This is an account of investigations carried out to determine the source of *Anopheles* mosquitoes that infested the residential quarters of the Palestine Potash Works situated on the western side of the north shore of the Dead Sea. The observations recorded are of exceptional interest.

A description is given of the topography and meteorology of this desert like valley 400 metres below sea level. The three anophelines found were *A. sergenti*, *A. multicolor* and *A. superpictus*. During the past 12 years the sea has receded leaving a high shoreline with brackish water outcrops along the western shoulder of the lake. During a search on this shoreline in the morning before sunrise puddles with *Culex* and *A. multicolor* larvae were found. When the place was revisited about 8.30 in the morning these puddles had disappeared and only after the removal of 10 to 15 cm. of gravel was the water with the larvae again disclosed. This nightly rise and daily fall of water level in sea shore puddles was noted several times during the investigations. The saline content of these puddles was 2.5 per cent. NaCl.

The persistence of *A. sergenti* after all nearby breeding places had been eliminated or controlled suggested that the mosquitoes were coming from the Feshka swamps from 4½ to 7½ kilometres south of the nearest Potash Works quarters. These swamps 1 km wide from the hills to the sea are fed by about 50 springs at the foot of the hills. Elevations of gravel and coarse sand obstruct the run-off of this spring water. The salinity of the water in the puddles and seepage areas varies from 0.25 to 0.65 per cent. NaCl. In the spring *A. sergenti* (predominating), *A. multicolor* and *A. superpictus* breed there in large numbers. In the autumn breeding in the gravel water outcrops is still more predominantly

A. sergenti with a very small percentage of *A. superpictus* and *A. multicolor*. *A. sergenti* continued to breed throughout the winter months of 1943.

In order to collect a large number of mosquitoes for a flight test 14 men spent a November night in the Feshka swamps seated in a circle with legs or thighs and arms bared. The mosquito alighting on the bare skin was taken in a test tube with the aid of a torch, preferably before biting. The mosquitoes thus caught were transferred to cages. By morning 2,600 mosquitoes had been captured all but 11 being *A. sergenti*. Early in the evening the first mosquitoes to arrive were culicines—after half an hour these disappeared and anophelines came on the scene. The anophelines came in waves throughout the night—the waves were independent of any change of wind—the night was almost windless.

For the flight test the mosquitoes were sprayed with gold dust, a finely powdered bronze preparation. One *A. sergenti* female with specks of gold dust on thorax and abdomen was captured 4.2 kilometres from the place of release on the second night after release.

Adult *A. sergenti* could be found in very large numbers in caves in the hill side adjacent to the Feshka swamps. Sometimes male mosquitoes formed 75 per cent. of the total catch. In the Kallia Hotel, at the Potash Works, about half the *A. sergenti* captured were males. Thus in the Dead Sea area male *A. sergenti* disperse for long distances and their presence does not indicate the proximity of breeding places. It is interesting that on several occasions *A. sergenti* were found in the open field near bushes in the early evening, but only when there was no wind or a very slight breeze. This indicates that *A. sergenti* rest in the open on their way to habitations in search of blood.

About 25 female *A. sergenti* whose thoraces were covered with the pollen of the plant *Anabasis articulata* were captured at distances of from 1 to 1½ kilometres from the nearest source of this pollen. The authors suggest that a coloured pollen, foreign to the area to be tested, might be a useful method of marking mosquitoes for flight tests.

Mites were found on about 20 to 25 per cent. of the mosquitoes taken in the Feshka caves and on about 3 to 5 per cent. of *A. sergenti* taken in the buildings of the Potash Works. Mites were found mostly on females, but also on males. The mites were identified as Hydrachnidae—fresh water mites of the Thya class. Very extensive search was made for the source of these Hydrachnidae. They were found on three occasions in Feshka waters and nowhere else. This finding is very strong evidence that *A. sergenti* found in the buildings of the Potash Works originated in swamps from 4½ to 8 kilometres away.

Norman White

BEKLEMISHEV, V. N. & GONTARVA, A. A. [Anophelogenous Landscapes of North-West Iran.] *Med. Parasit. & Parasitic Dis.* Moscow 1943 v 12 No. 5 17-32. [In Russian.]

Very little is known regarding the incidence of malaria and the distribution of the mosquito fauna in Iran. In 1941 the authors made a brief survey of the north-western part of the country with the object of determining the local epidemiological situation with special reference to the breeding places of anopheline mosquitoes. With Tabriz as the base, the survey was conducted along two routes—one, encircling Lake Urmia, the other through Miandeh, Zinjan, Karvin, Resht, Pahlavi, and back. This territory comprises the three main types of landscape of Iran—(1) the low lying coastal plain of the Caspian Sea, (2) the north-western uplands and (3) a small area of the central plateau.

The uplands represent an elevated plateau from 1 000 to 1 800 metres above sea level with mountain chains rising up to 4 000 metres. Natural vegetation is sparse but considerable areas are taken up by orchards and vineyards which are under perennial irrigation and by various food crops (chiefly wheat and rice) which are irrigated only twice a year. The anopheline fauna of this region includes *Anopheles superpictus* *A. maculipennis maculipennis* *A. m. sacharovi* and *A. bifurcatus*. Since the antimalarial organization in Iran is undeveloped and specific treatment of malaria is restricted to wealthier classes the bulk of the population remains untreated. On account of this the spread of the disease is governed by elemental factors chiefly depending on the altitude of the locality. In towns situated on the plateau itself (e.g. Kazvin Tabriz Rezayeh Khoj) the position is satisfactory. The low endemicity of malaria in these places is due to the presence of large arable areas with a limited water supply all the available water being directed from the streams into irrigation canals in which an intermittent flow is maintained. These conditions determine the small size of anophelogenous water collections with an insignificant mosquito population. However in towns situated in mountain valleys (e.g. Maragheh Mianeh Zanjan) the incidence of malaria is appreciable. Here the areas of arable land are relatively small but there is an abundant and constant supply of water which is used lavishly and allowed to overflow forming standing collections of water which provide numerous suitable breeding places for mosquitoes.

The Caspian coastal area is in complete contrast to the plateau region most of it representing a submontane plain lying at sea level and intersected by numerous rivers and streams which descend from the mountains while a considerable area is occupied by the delta of Sefid Rouda and the country between the rivers is frequently swampy. The climate in the plains is subtropical. Much of the cultivated land is taken up by rice as well as wheat and other crops and considerable numbers of cattle are kept. Except for towns human dwellings are scattered and apart from rice-fields there is no irrigation system but drainage ditches are numerous.

The predominant malaria vectors are *A. maculipennis* and *A. hyrcanus* while *A. superpictus* is absent. The distribution of mosquitoes is determined largely by the presence of *Gambusia* in most of the rivers and their tributaries as well as in the canals. Mosquito larvae could not be found in any of these streams but they breed mainly in closed water collections and in rice fields from which the larvivorous fish are absent. The authors were unable to obtain exact figures for the incidence of malaria in the areas visited by them but there seems to be a considerable decrease in the number of cases during the last few years which is attributed to the spread of the larvivorous fish since their introduction in 1936. [For other records of malaria in Iran see this *Bulletin* 1944 v 41 637-638.]

C. A. Hoare

BIELOGLAZOV G. G. [*Anopheles* in the East of the Mongolian People's Republic] *Med. Parazit. & Parasitic Dis.* Moscow 1943 v 12 No 5 33-6 1 fig [In Russian.]

The author reports the wide distribution of *Anopheles maculipennis messeae* throughout the eastern part of the Mongolian People's Republic where this mosquito occurs along the basins of the rivers Onon Uldsa Kerulen and Khalkhin-gol occupying the alluvial plains within the forest zones as well as the steppe country and intermediate landscapes. It is noted that the marked continental climate of this region with a severe winter does not prevent the preservation and multiplication of this species of mosquito. A detailed description is given of the geographical and climatic features of the country explored and of the mosquito fauna collected.

C. A. Hoare

COYA-GARCÍA, P. Penetración y dispersión en Venezuela de las especies *Anopheles* (*Nyctomyia*) *darlingi* y *Anopheles* (*Nyctomyia*) *albimanus*. *Rev. Sanidad Asistencia Social* Caracas. [Penetration and Dispersion in Venezuela of *A. darlingi* and *A. albimanus*] 1943 v. 8, No. 3, 467-72, 1 map.

Abstracted in *Rev. Applied Entom.* Ser. B. 1944 Dec. v. 32, Pt. 12, 230-31

RAMON, R. H. The Pathological Lesions in the Brain in Malaria. *Southern Med. J.* 1944 Dec. v. 37 No. 12, 687-94 7 figs. [35 refs.]

A general review

OLDFIELD, M. C. Traumatic Rupture of Malarial Spleen. *J. Roy Army Med. Corps.* 1945 Jan. v. 81 No. 1 27-8, 1 fig.

WOOD, P. The Erythrocyte Sedimentation Rate in Infective Hepatitis and in Malaria. *Brit. Med. J.* 1945 Jan. 6 9 1 chart.

The author describes the results of E.S.R. estimations done by the Wintrobe technique in a series of cases of early infective hepatitis and malaria. In 30 among 35 cases of infective hepatitis seen in the first 10 days of the disease the E.S.R. was under 10 mm in one hour in none of the cases did it exceed 20 at this stage. It was found to rise slowly and steadily during the period of bilirubin, and after the urine was bile-free it fell slowly to normal. In 23 of 32 cases of malaria the E.S.R. was between 20 and 60 mm in one hour. The author thinks that this test is of considerable value in differentiating the two diseases in their early stages.

In 84 per cent. of 72 measurements on cases of malaria between the 10th and 20th days of the disease the E.S.R. was above 10 mm in one hour. This helps to differentiate malaria from various short term fevers which may have been treated as clinical malaria, since the latter usually show a normal E.S.R. by the end of the first week.

J. A. R. Miles.

COLEMAN, Marion B. Vi Agglutinative Properties for *Bacterium typhosum* demonstrated following infection with Malaria Parasites. *J. Lab. & Clin. Med.* 1944 Sept. v. 29 No. 9 910-20. Summary appears also in *Bulletin of Hygiene*.

The sera of a high proportion of persons suffering from malaria were found to contain *Bact. typhosum* Vi agglutinins at titres ranging from 1/10 to 1/640. The sera of 23 out of 34 persons who were receiving malaria therapy and of 11 out of 28 persons suffering from naturally acquired malaria were positive. The author also confirmed the increased frequency of Vi agglutinins in the sera of individuals who had received heat-killed phenolized typhoid vaccine especially by the intravenous route. The presence of Vi antibodies was not directly related to the existence of H or O agglutinins.

The possible explanations of the observations are that malaria parasites possess Vi antigen or that the reaction is anamnestic, previously existing Vi agglutinins being re-stimulated by the malarial infection.

J. C. Crumckhorn.

RAYMOND, W. D. The Equivalent Quinine Index and Therapeutic Efficiency of Totaguina. *East African Med. J.* 1944 Oct. v. 21 No. 10 291-7.

Since 1942, totaguina has been prepared at Dar-es-Salaam. It contains all the cinchona alkaloids (the so-called Type I totaguina). The composition has

varied somewhat with different batches but three typical batches in 1944 had the composition —

	Per cent
Quinine	33-49
Cinchonidine	13-32
Cinchonine	6-10
Quinidine	0.1-1.5
Amorphous alkaloids	14-22
Moisture	2.6-4.5
Ash	2.7-4.1

It is calculated that 1 gm. of this product is equivalent to 0.5-0.58 gm. quinine base. 1 gm. quinine sulphate is equivalent to 0.75 gm. quinine base. The alkaloids are present as the free bases and before absorption they must be dissolved in the acid gastric juices converted into bihydrochlorides. Evidence from the literature is quoted to show that totaquina is practically as effective therapeutically as quinine while apart from a few exceptional batches in past records it is no more toxic. Assuming that the alkaloids of cinchona other than quinine are fairly effective in the treatment of malaria approximately twice as much active drug can be obtained from local bark as totaquina as would have been available as quinine moreover the yield of total alkaloids per acre from the local species of cinchona is about double that from the species *ledgeriana* preferred by quinine manufacturers. Accordingly it is urged that totaquina of this type is the most economical and effective means of obtaining the anti malarial action of cinchona bark.

F Hawking

EAST AFRICAN MED J 1944 Oct v 21 No 10 289-91 The Cinchona Alkaloids and Totaquina. [Editorial signed D.B.W.]

This is a comment on the paper by RAYMOND. The extraction of quinine from cinchona bark by orthodox methods is a complicated and therefore costly process involving two-thirds of the cost of production of quinine. Extraction of the alkaloids *en bloc* is simple and inexpensive. The Dar-es-Salaam totaquina is being sold retail at 2½ shillings per 100 tablets which is little more than half the retail cost of quinine tablets. Since economic factors play such a large part in the treatment among native populations in the tropics this aspect is of the greatest importance. The composition of totaquina should be standardized so that a uniform product is available. It should not be regarded as an inferior substitute for quinine but advantage should be taken of its lower cost to make it more widely available to those who need it. [This re-emphasis on the valuable antimalarial action of the cinchona alkaloids other than quinine is strongly supported by recent unpublished American work.]

F Hawking

MAEGRAITH B G BROWN G M ROSSITER R J IRVINE K N LEES J C PARSONS D S PARTINGTON C N RENNIE J L & HAVARD R E. Ammonia Excretion and the Clearance of Mepacrine. [Correspondence.] *Nature* 1944 Dec. 16 766

This is a preliminary notice about an investigation to enable the concentration of mepacrine in the urine to be estimated by examination of the urine. The concentration of mepacrine in the urine is proportional to the concentration of mepacrine in the plasma and to the concentration of ammonia in the urine if any two of these quantities are known the third can be calculated. Accordingly the equation is given

$$PM = \frac{1}{K} \frac{UM}{UNH_3}$$

in which PM is plasma mepacrine in microgm./litres UM is urinary mepacrine in microgm./litre UNH₃ is urinary ammonia in mgm. nitrogen/100 cc.

and $k=2.4$. By this means the concentration of mepacrine in the plasma can be estimated almost as accurately as by direct examination with Masen's method [this *Bulletin* 1945 v 42 8]. Probably the relation between the amount excreted in the urine and the amount of ammonia in the urine holds also for other basic drugs, e.g. quinine.

[Modern work on the use of mepacrine has placed great emphasis on estimation of the concentration of mepacrine in the plasma. Direct estimation of this concentration requires considerable experience and a well equipped laboratory including a good centrifuge and a delicate fluorimeter. On the other hand, simple methods are now available for the estimation of mepacrine and ammonia in urine using Lovibond discs. The above equation allows estimations of plasma mepacrine to be made in a simple field laboratory with a minimum of equipment.]

F. Hawking

HAYMAN J. M. Jr. Atabrine Pigmentation of the Sclera. *Bull. U.S. Army Med. Dept.* 1944 Nov No 82, 120-21

Pigmentation of the skin, especially around the mouth and on the hands and feet occurs in most people who take 0.6 gm. or more of atabrine [mepacrine] per week. The sclera, however are usually unaffected, but when staining does occur it is apt to be mistaken for jaundice. This happened in two persons seen by the author. The coloration was most intense around the limbus, in the part of the sclera exposed in the palpebral fissure and was fainter towards the fornices. In jaundice the reverse occurs, pigmentation being most intense in the fornices.

J. F. Corson.

WRIGHT C. I. & SABIXE Jean C. The Effect of Atabrine on the Oxygen Consumption of Tissues. *J. Biol. Chem.* 1944 Sept v 155 No 1 815-20 5 figs.

The effect of atabrin [mepacrine] in low concentrations, on the O_2 consumption of rat tissue slices suspended in phosphate-buffered saline pH 7.3 has been studied in the Bartlett apparatus in an atmosphere of oxygen. The drug at first increased the O_2 uptake by liver slices of a well nourished rat, and later inhibited it while in the case of liver slices from fasted rats the initial stimulation was small or absent. The O_2 consumption by rat brain or kidney slices was also inhibited. [These results are in contrast to those of MARTIN *et al.* *J. Pharm. & Exper. Therap.* 1938 v 65 158.] The addition of lactate, pyruvate, citrate, fumarate or malate failed to restore oxygen uptake after treatment of the tissues with atabrin, whereas the addition of succinate caused a sharp rise in its consumption. Atabrin did not interfere with the oxidation of p-phenylene diamine by tissue slices. The drug inhibited the oxidation of α -alanine by d-amino acid oxidase but the prosthetic group from the enzyme preparation counteracted its effects. The author suggests that the yellow enzyme systems are affected by atabrin.

J. D. Fallon

HAAS E. The Effect of Atabrine and Quinine on Isolated Respiratory Enzymes. *J. Biol. Chem.* 1944 Sept v 155 No 1 321-31 2 figs. [21 refs.]

In view of the inhibitory action of antimalarial drugs on plasmodial and tissue respiration [this *Bulletin* 1938, v 35 p 711 1942, v 39 p 367 and the preceding abstract (WRIGHT and SABIXE)] the effect of atabrin [mepacrine] and quinine on the isolated components of the respiratory enzyme system has been investigated as an aid to the understanding of the mode of action of these drugs. The components of this system are shown in an accompanying figure. The activity

of the various enzymes as well as their inhibition by atabrin and quinine were studied with the aid of spectrophotometric and manometric methods. Atabrin was found to inhibit cytochrome oxidase three times as effectively as quinine. The author however considered that the inhibition produced even by atabrin in the case of this enzyme was too small to account for its action on malaria parasites. Cytochrome *c* was not inhibited by this drug. Cytochrome reductase consists of a prosthetic group alloxazine mononucleotide (vitamin B₂ phosphate) along with a specific protein and is dissociable. Its activity was measured by its rate of reduction of cytochrome *c* and the inhibitory effect of atabrin on this reaction suggested that the latter reacted with the free protein arising from dissociation of the enzyme complex for which protein the prosthetic group also competed. An irreversible drug protein complex is apparently formed whereby respiration is interfered with a result which is dependent to some extent on temperature and largely on the concentration of the drug. One molecule of prosthetic group antagonized the action of 500 molecules of atabrin indicating that the specific protein has a greater affinity for alloxazine mononucleotide than for the drug. The author therefore suggests that certain alloxazine derivatives might prove efficient antimalarials by combining with specific enzyme proteins and at the same time fail to function as growth or respiratory factors for the malarial parasite. He also suggests that atabrin might be more effective in treatment if excess of vitamin B₂ phosphate were absent from the patient's diet. Atabrin was 12 times as effective as quinine in inhibiting cytochrome reductase. The activity of the prosthetic group (triphosphopyridine nucleotide) in glucose-6-phosphate dehydrogenase was not inhibited by atabrin while that of the protein part of the complex was inhibited but remained unaffected by quinine. Some experiments suggested that the action of atabrin might alternatively be due to displacement of substrate rather than of the prosthetic group competing with it for enzyme protein. Quinine shows a less marked inhibition of isolated respiratory enzymes or of malaria parasite respiration than does atabrin and the author believes that the mechanism of action of the two drugs in malaria may not be the same. Attempts to isolate any of the known respiratory catalysts from *P. knowlesi* parasites which had been dried for some time proved unavailing.

J D Fullon

ALLEN C. Diagnosis of Psychotic Symptoms in Atabrin Intoxication [Correspondence] *Brit Med J* 1944 Dec. 23 831

Patients who have been given large doses of atabrin for malaria may develop certain mental symptoms— a florid hypomanic state sometimes with vague paranoid delusions often with grandeur visual hallucinations are absent. When this occurs general paralysis is suspected and a Wassermann test is done and may give a positive result due to malaria. The serious results that may follow such a mistaken diagnosis are obvious. The author recently met with such a case in a man who had returned from North Africa his wife was told that her husband was syphilitic and that she and their children were possibly also infected.

J F Corson

BIRD W. Atabrin and Plasmoquine in the Treatment of Benign Tertian Malaria. [Abstract.] *J Malaria Inst of India* 1944 June v 5 No. 3 395-6

WEST J B & HENDERSON A B. Plasmochin Intoxication. *Bull U.S Army Med Dept* 1944 Nov No 82 87-89 3 graphs [Refs. in footnotes]

A review is given of the literature dealing with the toxic effects of pamaquin (plasmochin). FISCHER and WEISE [this *Bulletin* 1928 v 25 135] considered

that 0.03 gm. daily was the maximum dosage of this drug which should be given. The present paper is based on the treatment of 846 young males previously infected with *P. falciparum* in a tropical area. Each was given 10 grams (0.67 gm.) quinine sulphate three times daily for three days or until the fever was controlled, and then 0.1 gm. mepacrine three times daily for five days. After a rest period of two days, the patient was given pamaquin 0.01 gm. three times daily for five days. The patients were ambulatory. Twenty-four of the 846 men (2.85 per cent.) had to be readmitted to hospital for what appeared to be pamaquin intoxication. The smallest amount causing toxic symptoms (four patients) was 0.06 gm. The symptom complex consisted of jaundice (20 cases) abdominal pain (19 cases) colicky and recurrent responding to anti-spasmodics, slowest of all the symptoms to disappear (in five cases it continued for four weeks after the drug was stopped). Could some of this be due to psychological causes? anaemia, r.b.c. below 4 million per cmm. (19 cases) headache (16 cases) dull persistent occipital, relieved by acetyl salicylate weakness (14 cases) and dizziness (11 cases). Two cases developed mild toxic psychoses. Liver and spleen were normal and there was no methaemoglobinæmia. In the blood of 22 patients examined there was increased icteric index with or without hyperbilirubinaemia. In nine cases the urine contained albumin or bile sometimes both in four cases blood was detected by benzidine tests in six urines examined urobilinogen was found.

All the patients were taken into hospital and treated by palliative methods including an increased intake of fluid. The time spent in hospital was 7-72 days average 25 days. The authors consider a dose of 0.01 gm pamaquin twice daily for two days as sufficient to render the blood non-infective for mosquitoes and to be free from toxic effects.

[The authors give their reasons for believing that these symptoms were due to intoxication by pamaquin rather than to some other cause but it must be admitted that the latter possibility is difficult to exclude. At a military hospital in England over 200 men with relapses due to *P. vivax* were treated with 10 grams quinine and 0.01 gm. (of base) pamaquin three times daily for 10 days. No toxic symptoms apart from two cases of gastro-intestinal disturbances were observed and the proportion permanently cured by this course was greater than that cured by mepacrine.]

F. Hacking

LEITMAN, M. Z. 'Prophylaxis with Acriquine and Plasmocide in an Area of High Malaria Incidence in a Rice-Field Zone of Uzbekistan.' *Med. Parasit. & Parasitic Dis.* Moscow 1943, 12, No. 5, 62-72. [In Russian.]

The author describes the results of mass chemotherapeutic treatment of malaria in a number of settlements of the Tashkent Province (Central Asia), the population of which is engaged in agricultural work in the vicinity of numerous rice-fields representing the main mosquito-breeding places in this locality. The prevalent malaria vectors are *Anopheles maculipennis sacharovi* (87.2 per cent.), *A. superpictus* (10.9 per cent.) and an insignificant proportion of *A. pulcherrimus* and *A. byrsoni*. An examination of 1,595 inhabitants for malaria, in 1938 revealed the following figures: endemic index 43.6 spleen index 40 parasite rate 8.6 Ross index 2.9. This population was divided into two groups: (1) an experimental group of 838 persons, and (2) a control group of 757 both comprising persons of different sexes and ages in comparable proportions. The first group underwent suppressive treatment with 0.2 gm. acriquine [mepacrine] + 0.04 gm. plasmocide [pamaquin] given daily for two days in succession followed by an interval of three days (this was the dose for adults children receiving smaller amounts). This cycle was repeated regularly. In the control group therapeutic treatment with acriquine was applied

to those persons who became infected. Some difficulty was experienced with children under the age of eight owing to their inability and disinclination to swallow the acrid acríquine tablets. Such cases as well as refractory adults were treated prophylactically with sugar-coated quinine sulphate pills.

The whole investigation occupied a year in the course of which the results were assessed on four occasions. A comparison of the experimental and control groups showed that prophylactic treatment with acríquine and plasmocide brought about a marked diminution in the number of cases of malaria in the former. Treatment of children and others with quinine sulphate was ineffective.

C. A. Hoare

EDDEY L. G. *Spray-Killing of Mosquitoes in Houses—a Contribution to Malaria Control on the Gold Coast.* *Trans. Roy. Soc. Trop. Med. & Hyg.* 1944 Dec. v. 38 No. 3 167-68 1 map & 2 charts. Discussion 188-97 [GORDON R. M. JAMES S. P. COLLINGWOOD F. C. WHITTINGHAM H. BLACKLOCK D. B. KAUNTEE W. H. HACKETT C. J. WIGGLESWORTH V. B. EDDEY L. G. (in reply by air letter)]

The harbour and airport at Takoradi in the Gold Coast Colony assumed great strategical importance in 1941. The sudden arrival of large numbers of susceptible European personnel necessitated very vigorous malaria control measures. During the rainy season of 1941 the monthly malaria morbidity rate attained 216.8 per 1,000. Nearby townships constituted the chief danger. It was therefore decided to supplement the usual antilarval and individual prophylactic measures by spray-killing adult mosquitoes in all houses in the central part of Takoradi (population 10,505) and in a group of coastal villages between Takoradi and Sekondi (population 7,162). The paper describes how this work was carried out between November 1942 and November 1943 and the results obtained.

There were some 7,050 rooms to be treated, nearly all of which possessed solid walls, close-fitting doors and louvred or close-batten windows. Two rooms were sprayed at a time: two sprayers worked inside each room and one outside the latter spraying over the previously closed window and door apertures. After the spraying the rooms were left closed for 15 minutes, then all dead or stupefied mosquitoes were swept up and their numbers recorded. The inhabitants were cooperative, appreciating the marked diminution of the mosquito nuisance, locked and consequently inaccessible rooms were less than 10 per cent of the total number during 1943. The onset of the rainy season was followed by a great increase in the numbers of anophelines killed. *A. gambiae*, the chief vector, was much the most prevalent species. *A. funestus* was only occasionally found and *A. pharoensis* and *A. paludis* very rarely.

In the beginning the insecticidal mixture used was 1 ounce of cresol in one gallon of kerosene, sprayed with a slit-gun type of domestic sprayer. Subsequently a limited use was made of dry pyrethrum dust, a kerosene extract of pyrethrum, and of pyrethrum aerosol. All methods were effective, but pyrethrum aerosol is the insecticide of choice and pyrethrum kerosene next best. Limited supplies and high cost made the extended use of dry pyrethrum dust impracticable. The dust has a useful repellent effect. There was but little difference in the over-all cost of spraying with the three liquid preparations: pyrethrum-kerosene, creso-kerosene and pyrethrum aerosol. The cost was slightly over one penny per head per week.

It was not possible to measure with accuracy the degree of malaria control attributable to the spraying. The malaria incidence in one group of Service personnel in 1943 was 42.7 per cent, and in another 34.2 per cent, of the corresponding incidence in 1942. The general malaria rate of the Services throughout

the Gold Coast was 50 per cent. lower in 1943 than in 1942. These figures suggest that local measures in Takoradi made a noteworthy additional contribution to the protection afforded by anti-malarial measures that were applied throughout the Colony. Further evidence of the protection given by spraying was provided in one village by a much lowered infant infection rate.

In the discussion, Colonel S. P. JAMES expressed gratification that spray killing adult mosquitoes, a method of malaria control that was advocated by the Malaria Commission of the League of Nations 20 years ago is being increasingly used. It is to be expected that still better results will be obtained when supplies of the new synthetic insecticide DDT become generally available. Rooms sprayed with DDT remain toxic to mosquitoes for several weeks, and mosquitoes are not repelled by it. It promises to bring nearer the eradication of malaria as the greatest scourge that the world has ever known.

Air Marshall Sir H. WHITTINGHAM considered that the greater reduction in malaria incidence in one group of Service personnel in Takoradi than in another was indicative of the value of house-screening as a measure of malaria control.

Professor D. B. BLACKLOCK referred to an observation made by the author that in some of the villages where miles of drains had been cut, there had been an increase of anophelines in the houses. Silting of earth drains with sand and consequent pool formation—and damage to drains by cattle and by man—create innumerable anopheline breeding places unless the drains receive constant supervision. These surface drains should be replaced by sub-surface drainage. The cost of spraying (a penny per head per week) may seem small but it may well be prohibitive for the family of an African labourer. *Norman White*

ELLIS, M. M., WESTFALL, B. A. & ELLIS, M. D. Toxicity of DDT (Dichloro-Diphenyl Trichloroethane) to Goldfish and Frogs. *Science* 1944 Nov 24 477

Goldfish and frogs are more susceptible to DDT than rats, cats and rabbits. Single doses of 63–200 mgm. per kgm. were lethal when dissolved in olive oil and incorporated in food pellets which were swallowed by gold fish weighing 6–10 gm. In this range the mortality was 55 per cent. and was correlated roughly with the size of the dose. Frogs injected with DDT in olive oil were killed in 4–72 hours by single doses of 150 mgm. per kgm.

These findings have a bearing on the use of DDT against mosquito larvae.

Charles Wilcocks

TALLAFERRO, W. H. & TALLAFERRO, LUCY G. The Effect of Immunity on the Asexual Reproduction of *Plasmodium brasilianum*. *J. Infect. Dis.* 1944 July–Aug. v 75 No 1 1–32, 1 pl & 6 graphs [25 refs.]

In 1934 the authors (*this Bulletin* 1935 v 32, 425) reported upon the behaviour of *Plasmodium brasilianum* in Central American monkeys. It was noted that the merozoite mean per segmenter varied between 8.5 and 10 and the 3-day periodicity was regular throughout the infection except at the time of the crisis or decrease in parasitaemia, when (1) the asexual cycle sometimes took four or five days instead of three days, (2) the average number of merozoites per segmenter sometimes decreased and (3) the mean size of the segmenters sometimes decreased "there being a correlation between the size of the segmenters and the number of merozoites." It was concluded that the basic rate of reproduction was constant except at the crisis and that the various aspects of an infection were the result of a differential mortality of parasites during the entire infection, on which was superimposed a temporary retardation of reproduction during some crises. The results presented in the paper under review furnish more exact data and modify the original conclusions to some

Blackwater Fever

extent They are based on the detailed study of *P. brasilianum* in four *Cebus capucinus* and on a re-examination of 60 similar infections in 23 white-throated monkeys (*Cebus capucinus*) 6 red spider monkeys (*Ateles geoffroyi*) 9 black spider monkeys (*Ateles darsenisi*) 10 howler monkeys (*Alouatta palliata*) six marmosets (*Leontocebus geoffroyi*) and six night monkeys (*Aotus zonalis*)

It was found that significant changes occurred (1) in the synchronism in all marmosets and night monkeys during the entire infection and in some spider and howler monkeys during the parasite decline (2) in the average number of merozoites per segmenter in major and minor broods during the entire infection in the majority of monkeys and (3) in the periodicity and morphology of the parasites at the time of these variations from a merozoite number of 8.5 to 10 a species. The extent of these variations from a merozoite number of 8.5 to 10 a 72 hour periodicity and a high degree of synchronism are illustrated in a series of tables and charts. In certain cases when at the crisis or commencement of decline the 72 hour periodicity is extended to four to five days a minor brood of parasites may be split off a fact which may account for changes in type of fever curve during the course of malaria in man. Similar findings were obtained during the acute rise parasite decline and development of relapses.

The foregoing results are interpreted in terms of immunity. Natural immunity which functions alone during the acute rise in the infection is associated with a marked death of parasites and sometimes with a sporadic variation in asexual reproduction. Acquired immunity with continued natural immunity comes into play at the crisis and brings about a heightened death of parasites and especially during sharp crises a marked lowering of the rate of reproduction. The lowering of the rate of reproduction at these crises is due to (1) a derangement of the asexual cycle involving a lack of synchronism and a lengthening in some segmenters as well as the appearance of degenerate crisis forms. These changes are regarded as due to the effect of parasitocidal antibodies though it is recognized that the changes in the host resulting from the intense antigen-antibody reaction at the time of the crisis may to some extent also be responsible. A series of figures illustrates the various types of segmenters (schizonts) observed in *P. brasilianum* infections including the evidently abnormal forms which found at the time of crisis.

C. M. Wesson

BLACKWATER FEVER

АПОКСKY Н. П. [The Treatment of Blackwater Fever by Blood Transfusion.]
Med. Parasit. & Parasitic Dis. Moscow 1943 v. 12 No 5 72-4 [In Russian]

The author describes three cases of blackwater fever one with M.T. parasites in the blood another with a history of malaria in the past and the third who had never suffered from malaria or taken quinine. All three patients who manifested severe symptoms showed dramatic improvement after blood transfusion (200 cc.) and were discharged as cured. It is concluded that in blackwater fever blood transfusion is indicated in all cases and should not be delayed until severe symptoms make their appearance. This form of treatment is regarded as fundamental and not merely supplementary. C. A. Hoare

TRYPANOSOMIASIS

STEFANOPOULO G & ERIST J Méningo-encéphalo-myélite de la souche blanche due à une souche neurotrope de *Trypanosoma gambiense* (Meningo-Encephalo-Myelitis of the White Mouse due to a "Neurotropic" Strain of *Trypanosoma gambiense*). Bull Soc Path Exot 1943 Jan. 13 & Feb 10 v 36 Nos. 1-2 43-5 8 figs. on 3 pls.

The authors have examined white mice infected with a strain of *Trypanosoma gambiense* that had been found by ROUBAUD and PÉGVOST (this Bulletin 1942 v 39 234) to have neurotropic properties for mice. These animals have been generally considered to get a blood infection only. Of 19 infected mice 9 showed symptoms of paralysis and of these 5 had been inoculated intraperitoneally and 4 intracerebrally. The former showed paralytic symptoms in different animals 68 to 189 days after inoculation the latter after 41 to 223 days. Three of the mice died spontaneously after 23, 41 and 44 days and the other six were killed from 1 to 59 days after paralysis appeared. In mice which did not develop paralysis the infection had a shorter course and trypanosomes were more constantly present in the blood.

At autopsy the lymph glands were found much enlarged but the spleen and liver showed little macroscopic change. The brain was hyperaemic and in some cases oedematous. The histological lesions of the central nervous system are described: they resembled those recorded by PLUMMER (Proc Roy Soc, 1907 Ser B v 79 85) in rats (which become paralysed) and by other workers. Perivascular infiltration by lymphocytes and plasma cells and meningitis are present but the authors found no changes in the choroid plexus or ependyma nor did they see any molar cells of MORR (Rep Sleeping Sickness Comm. Roy Soc 1908 No 7 15). The kidneys and liver also showed lymphocytic infiltration similar to that described by PETTIT (Sleeping Sickness Bulletin 1911 v 3 264) who called it lymphoid transformation of the liver.

In discussion ROUBAUD suggested that the mouse may perhaps serve to test the greater or less tendency of different human strains of trypanosomes to infect the nerve centres.

BROWNING C H BROWNING P & ROSS J V M. A Phenanthridinium Compound of Morgan and Walls as a Chemotherapeutic Agent in Experimental Infections with *T. congolense*. J Path & Bact 1940 v 50 371-2.

It was found by BROWNING and his co-workers (this Bulletin 1938 v 35 344) that one of a series of phenanthridinium compounds, 7-amino-9-(β -amino-phenyl)-10-methylphenanthridinium chloride possessed curative action in mice infected with *Trypanosoma congolense*. Further work has shown that infection may be cured with 1/60-1/100 of the maximum tolerated dose given subcutaneously. On the other hand *T. brucei* infection was cured only by a dose near the maximum. Prophylactic action against *T. congolense* was found to be slight.

As regards toxicity a dose of 0.005 gm. per kgm. intravenously as a 1/400 solution caused no illness. 0.013 gm. might be fatal at once or this dose or 0.01 gm. might cause illness followed by rapid recovery and no later ill effects.

J F Corson

BROWNING C H & CALVER K. M. The Effect of the Stage of Infection on the Chemotherapeutic Response of *T. congolense* and on the Immunity following Cure. *J Path & Bact* 1943 v 55 No 3 393-4

Two strains of *Trypanosoma congolense* were used in a study of the biological aspects of cure of the infection in mice by 7-amino-9 (β -aminophenyl)-10 methylphenanthridinium chloride [see BROWNING BROWNING and ROSS above p 258]. One of the strains no I usually caused relapsing infections while in the other no II which caused a more severe illness numerous trypanosomes persisted in the blood until death occurred after a few days to several weeks. Treatment was more effective at the acme stage [when trypanosomes are abundant] than earlier and this suggests that an immunity reaction plays a significant part in the cure.

Infections produced by inoculation from a chronic infection of either strain required much larger doses for cure than infections produced by inoculations of the same strains at the acme stage. If in animals inoculated with acme trypanosomes treatment is delayed until the infection has become chronic cure may be difficult.

The immunity produced after cure with the drug was much more solid in strain I than in strain II infections. There was no immunity however to the trypanosomes of chronic infection and there was no cross immunity between the strains. When a chronic strain was passed at the acme stage through a series of fresh mice it sometimes regained its acme character as shown by the immunity test by the 5th passage but on the other hand the chronic character might persist for 7-11 passages or more.

With this drug the ultimate chance of cure in a relapse appeared to be as good as in the initial infection. occasionally evidence of drug resistance was obtained.

The authors suggest that under field conditions therapeutic results may depend on the strain of *T. congolense* the stage of infection and other factors and that failure to cure relapses does not necessarily imply drug resistance. The part played by cyclical development in the tsetse fly is of course not indicated by these experiments.

J F Corson

CARMICHAEL, J & BELL, F R. A Study of the Therapeutic Action of the Phenanthridinium Compound 897 against *Trypanosoma congolense* Infection in Cattle. *J Comp Path & Therap* 1944 Jan. v 54 No 1 49-52

The new drug S 897 7-amino-9 (β -aminophenyl) 10 methylphenanthridinium chloride having been shown by BROWNING *et al* [see above] to cure *T. congolense* infection in mice the authors tried it in experimental infections of cattle. two laboratory strains of *T. congolense* were used and the cattle were presumably infected by inoculation. The toxicity of the drug was first tested in eight cattle the highest non toxic dose intravenously was 3 mgm. per kgm. body weight which owing to the low solubility of the drug required a volume of solution that was hardly practicable for general use. The drug appeared to produce no change in the blood of the animals.

Six cattle were infected with *T. congolense* and four were given a dose of 2 mgm per kgm when they were in the chronic stage of the disease. all were cured i.e. they became well, their blood showed no trypanosomes on daily examination for four months and subinoculation into susceptible cattle proved negative.

In a second experiment a herd of 40 infected cattle was divided into five groups of eight animals and treated with a dose of 2 mgm. per kgm. by various routes the results are shown in Table III —

TABLE III

Route of Administration	Result
1. Intravenous	3 cured, 4 relapsed, 1 death intercurrent infection.
2. Subcutaneous	2 cured, 5 relapsed, 1 death intercurrent.
3. Intramuscular	1 cured, 7 relapsed.
*4. Intravenous and subcutaneous	1 cured, 7 relapsed.
5. Intravenous and intramuscular	4 cured, 4 relapsed.

Half the total dose was given by each route.

The initial treatment cured 11 animals, 27 relapsed, and 2 died from intercurrent conditions. The relapsed cases were re-treated by an intravenous injection of 2 mgm. per kgm given 44 days after the first treatment. 22 were cured. All the relapses had occurred 14-29 days after treatment. Five (all infected with the same strain) which again relapsed were similarly re-treated after another 49 days but again relapsed and a fourth treatment was also ineffectual.

Intramuscular injections caused stiffness and lameness.

The authors consider the intravenous or the intravenous plus the intramuscular route to be best. An experiment showed that a dose of 2 mgm. per kgm. protected up to 48 hours against a very heavy inoculation of trypanosomes.

J. F. Corson

CARMICHAEL, J. & BELL, F. R. The Use of a New Phenanthridinium Compound 1553 in the Treatment of *Trypanosoma congolense* Infection in Cattle. Reprinted from *I et Record* 1944 Dec 16 2 pp.

A new phenanthridinium compound (1553)—2,7-diamino-10-methylphenanthridinium bromide—was stated by BROWN, D.C. (private communication) from whom the authors received it to be more active than S 897 (above) and to cause less induration at the site of injection. A 4 per cent. solution can be obtained easily in hot water and the drug remains in solution on cooling; the solution has a port-wine colour.

The authors tested the drug on bumpy cattle (zebu) infected with *Trypanosoma congolense* by subcutaneous inoculation three recently isolated virulent strains being used. In the first experiment, a dose of 2 mgm. per kgm. was given as a 2 per cent. solution when trypanosomes were numerous in the blood; the results are shown in Table I.—

TABLE I.

No. of zebras	Route of administration	Cures	Relapses
4	Intramuscular	4	—
1½	Subcutaneous	3	4
4	Intravenous	4	—

The trypanosomes disappeared from the blood within 24-48 hours. The four relapses were again treated with the same dose subcutaneously between the 19th and 24th days after the first injection and all were cured, the test of cure being the blood was free from trypanosomes on daily examination for four

months the blood returned to normal the bodily condition improved and inoculation of mice was negative. Intramuscular injections caused painful swelling and lameness which persisted for some weeks but there was no sloughing subcutaneous injections however caused very little reaction.

In the second experiment the drug was given subcutaneously (with various slight modifications) to 19 zebras with chronic *T. congolense* infection the details and results are shown in Table II —

TABLE II.

Dose mgm. per kgm	Percentage Solution 1333	
	2 per cent	1 per cent.
1.0	4 4C	4 4C
1.5	4 4C	4 4C
2.0	— —	3 3C

C=Cured.

Only one animal showed a local reaction it had received a 1 per cent solution and massage was not done

The experiment shows that the compound has very high curative properties for *T. congolense* infections all the 39 cattle being cured. The toxicity of the drug was not investigated but the authors believe that it is low

J F Corson

SEAGER L. D. Transmission of *Trypanosoma equiperdum* to the Duck. *Science* 1944 Nov 10 428

The author injected *Trypanosoma equiperdum* in doses of 500 millions per kgm. of body weight intravenously into ducklings one week old. Four groups [number not stated] showed no trypanosomes in the blood on examination during 8-12 days two died on the 14th and 15th days respectively and the latter had numerous trypanosomes in its blood mice subinoculated from it died of trypanosomiasis on the 4th day after inoculation. Ten other week-old ducklings were also inoculated intravenously and observed for 18 days two showed trypanosomes in the blood on the 10th day and died of trypanosomiasis on the 12th and 14th days respectively. The blood of the other eight ducklings showed no trypanosomes but when it was inoculated intraperitoneally into mice it produced fatal infections in all.

The author states that the implications of these findings as to possible avian reservoirs of similar mammalian parasites is obvious. [Several workers have transmitted human and other mammalian pathogenic trypanosomes to various species of birds—fowls geese ducks guinea-fowl francolins—see *Sleeping Sickness Bulletin* 1909 v 1 No 5 201 1912 v 4 No 39 277 this *Bulletin* 1931 v 28 921 1932 v 29 837 1933 v 30 454 1935 v 32 710 Avian blood has been found in nature in tsetse flies.] J F Corson

LEISHMANIASIS.

RAMAN T K. Kala Azar in Non-Endemic Areas. *J Indian Med. Ass.* 1944 Oct. v 14 No 1 pp 8 & 7

The author reports that during 1933-1942 twelve cases of kala azar were admitted to the King George Hospital Vizagapatam, which is not an endemic centre for this disease. Ten of the cases had their origin in Madras or Calcutta but in two the patients had never left Vizagapatam or its neighbourhood. It was difficult to account for infection in these two cases. The suggestion is made that it was contracted orally. The aldehyde test was carried out in 200 unselected cases in Guntur where no cases of kala azar had been met with. It was strongly positive in 4 per cent. of these moderately positive in 7 per cent. and slightly positive in 8.5 per cent. In none of these cases was it possible to establish a diagnosis of kala azar though every test was applied. Three similar cases with strongly positive aldehyde test and enlarged spleen were seen in Vizagapatam. No leishmania could be found by spleen puncture. C M Wenyon.

WERTHEIMER E. & STEIN L. The Cold Susceptible Globulin Fraction of Pathologic Sera. *J Lab & Clin Med* 1944 Oct v 29 No 10 1082-9

In an earlier paper (see this Bulletin 1942, Vol 39 p 747) the authors showed that the serum from cases of kala azar in human beings and dogs contained a protein fraction which came out of solution as a flocculent precipitate when the serum was kept at a temperature of 7-11°C. It was named the Cold Fraction (C.F.) and was found to be related to euglobulin. In the present paper an account is given of further studies on this C.F. It has been found that for complete separation an exposure to cold for three days is necessary. There are five degrees or types of separation as follows: turbidity light precipitate, flocculent precipitate, precipitate capable of estimation by quantitative methods and a different precipitate found as a layer on the surface. In five cases of kala azar in human beings and in three cases in dogs the C.F. was present in varying degree as shown in tables. It was noted that if as a result of treatment clinical cure was obtained (with a rise in the albumin of the serum a fall in the globulin particularly the euglobulin, and a decrease in the intensity of other abnormal serological reactions) the C.F. nevertheless persisted for long periods. The question arises as to whether cure can be regarded as having taken place in such circumstances. Further observations on a more extended scale will be needed to supply the answer. It was shown in cases of kala azar in dogs that the abnormal protein hunger englobulin C.F. and other fractions persisted in spite of chronic protein hunger and extensive loss of blood. The C.F. has been shown to be present in cases of endocarditis lenta while in lipoid nephroses the final phase of chronic uraemia and in cirrhotic changes of the liver a C.F. of a peculiar nature occurs in the serum. It is stated that in 13 cases of *Leishmania cutis* (Jericho rose) C.F. of grade 2 was present in one case. [It is evident that the term *Leishmania cutis* is intended for *leishmaniasis cutis* and not for a new species of *Leishmania*] C M Wenyon

GOODWIN L G. The Chemotherapy of Experimental Leishmaniasis. I. The Spleen as an Index of Infection in the Syrian Hamster. *Trans Roy Soc Trop Med & Hyg* 1944 Nov v 38 No 2, 151-60 2 figs. [20 refs.]

With the object of working out a reliable test for therapeutic activity of drugs against *Leishmania donovani* the author has investigated the possible

errors associated with the method adopted by ADLER and TSCHERNOMORETZ [this *Bulletin* 1940 v 37 775 1942 v 39 173 & 748] which consisted in making stained smears from portions of spleen removed from infected hamsters before and after treatment and counting the number of parasites per hundred cell nuclei. The possible sources of error are the counting of an inadequate number of parasites and nuclei uneven distribution of parasites in the spleen sporadic changes in the intensity of infection the drug may not act equally on all parts of the spleen. These various sources of error are carefully investigated by the author. It was determined that in spleens in which there occurred 50 or more parasites per 100 cell nuclei a fair estimate of the degree of infection can be obtained by counting the parasites against 250-500 nuclei. For infections of less than 10 parasites per 100 nuclei 500 to 1 000 nuclei must be counted. It was also found that there was a fairly even distribution of parasites throughout an infected spleen while untreated animals show a steady increase of infection which may be very rapid after spleen biopsy. Single subcutaneous doses of organic antimonials have been shown to have a measurable effect upon parasite counts in the spleen an effect which is uniform throughout the organ. The films for counting purposes were made by dahhing on slides the cut surfaces of portions of spleen removed by biopsy. They were stained by Giemsa stain. The author concludes that his observations form a sound basis upon which therapeutic potency tests may be designed. C M Wenyon

PATEL J C Six Cases of Kala-Azar in Bombay Sodium Antimony V Gluconate In Its Treatment, *Indian Physician* 1944 Nov v 3 No 11 319-27 [26 refs.]

In this paper the author describes the treatment of six cases of kala azar in Bombay. All were imported from the United Provinces Bihar or Bengal. Three of the patients were adults and three children 8 10 and 14 years of age respectively. Diagnosis was established by the finding of leishmania in smears or leptomonads in cultures from sternal puncture material. All cases were treated with sodium antimony V gluconate (stibatin of Glaxo Laboratories). It was found that the adults would tolerate 10 daily injections of 20 cc. of the solution which is of such strength that 1 cc. contains 20 mgm. of metallic antimony. Accordingly after trials in the first case treated this dosage was adopted for the other two adults one receiving the 10 doses intravenously and the other intramuscularly. As regards the three children the youngest had intravenous injections of 12 cc. for 10 days (120 cc.) the one 10 years of age 15 cc. intravenously for 10 days (150 cc.) and the eldest 1 dose of 5 cc. and nine doses of 6 cc. intramuscularly (59 cc.) during ten days.

In no case were any toxic symptoms noted and cessation of symptoms and improvement in general health occurred in all. One child, 10 years of age, died of tuberculous meningitis four months after treatment. There was no indication of kala azar at the time of death. Four of the other five patients followed for six or more months are regarded as permanently cured. One is still under observation. It is noted that in one case a positive culture was obtained from sternal puncture material after the course of treatment has been completed. Six months later culture was negative and a permanent cure registered.

The author concludes that sodium antimony V gluconate is the drug of choice in the treatment of kala azar as it has so many advantages over neostibosan and urea stibamine. He considers that it should be given extensive trials in endemic areas. A more concentrated solution in which 1 cc. contained 50 mgm. of the drug in place of the usual 20 mgm. had been tried. It seemed that the advantages of a reduction in bulk of fluid to be injected was probably counter-balanced by the greater amount of antimony required. C M Wenyon

FULLER, A. T. A Colour Reaction for Aromatic Amidines. [Correspondence.]
Nature 1944 Dec. 16 773

DEVINE [this *Bulletin* 1944 v 41 830] described a method for the colorimetric determination of stilbamidine based on the observation of ERLY & ROVIZIO (*Jl Amer Chem Soc* 1935 v 57 1353) that certain aromatic diamidines, heated with glyoxal in alkaline solution yield coloured derivatives. In the present independent investigation the method has been modified and made more sensitive and reliable by heating in a borate buffer at pH 9. It has proved suitable for the estimation of aromatic amidines at a dilution of 1 in 100,000. The buffer was prepared from 4 gm boric acid neutralized in hot solution with caustic soda to pH 9 and diluted to 100 cc. The glyoxal reagent was used as the sodium bisulphite in 0.5 per cent. aqueous solution. When carrying out an estimation a few cc of the amidine solution roughly neutralized were mixed with about 1 cc. of each of the reagents, and the mixture maintained near the boiling point for a few minutes or left on the water bath for 10 minutes, when a pink or magenta colour was produced. The best development of colour was obtained with approximately two molecules of the reagents to one of amidine. The reaction which is specific for an unsubstituted aromatic amidine group is inhibited by excess of glyoxal. The reaction does not take place with compounds in which one or two methyl groups are attached to the nitrogen of the amidine group nor with guanidines, biguanidines amines or aliphatic amidines. In some cases the reaction products with aromatic amidines showed fluorescence in ultra violet light at a dilution of 1 in 100 millions. J. D. Fulton

SEN GUPTA, P. C. Phenamidine in the Treatment of Kala-Azar [Correspondence.]
Indian Med Gaz 1944 Oct. v 79 No. 10 806.

COSTA, O. G. Metastatic Form of American Leishmaniasis. *Arch. Dermat & Syph*
 1944 Nov., v 50 No. 5 328, 2 figs.

Report of a case.

FEVERS OF THE TYPHUS GROUP

VAN ROOYEN C. E., BOWIE J. H. & KRICKORIAN K. S. Typhus Research in Egypt, Palestine, Iraq and Iran. *Trans Roy Soc Trop Med & Hyg* 1944 Nov. v 38 No. 2 133-49 [16 refs]

This paper is a shorter and much more attractive version of the one reviewed in this *Bulletin* 1945 v 42, 194. It is welcome because the previous article is not likely to be accessible to many workers on the subject.

After extensive trials of the Weil-Felix and rickettsia-agglutination tests the authors make the following statement—"On the 4th or 5th day the Weil-Felix titre is invariably below the normal titre of 1-100 on the 8th or 7th day a low titre 0X19 and similar positive rickettsial agglutination occasionally may be observed to a serial dilution of 1-200. On the 8th and 9th day the two reactions are usually positive to a titre of 1-400. From the 10th to 14th day both reactions become strongly positive and many vary from 1-800 to 1-6400. From the 14th to 21st day very high titre 0X19 and rickettsial-agglutination is invariably present in severe epidemic typhus. The rickettsia reaction is held to be superior to the Weil-Felix in its ability to differentiate between epidemic and murine typhus, but on the other hand the antigen is

very costly and the flocculation is difficult to observe when the titre of the reaction is low so that the best results are obtained between the 10th and 15th days

A table in the paper gives the various titres observed in 119 cases all but three of which were diagnosed as murine or epidemic on the strength of the higher titre agglutination to one or other of the two types of rickettsiae. In most of the cases the differences in titre were great but among the last 23 cases diagnosed as murine there were seven in which the murine titre was only twice as high or less than twice as high as the epidemic titre.

The following extract from the table shows the results obtained in one special group of six consecutive cases which occurred within a period of seven days in July 1943 at Quassassim.

Serial number	<i>Proteus</i> OX19 titre	Epidemic rickettsia titre	Murine rickettsia titre	Diagnosis
94	500	1 600	400	Epidemic
95	200	100	500	Murine
96	3,200	800	1 600	Murine
97	300	300	800	Murine
98	200	500	800	Murine
99	400	400	500	Murine

[This group is exceptional but it suggests the possibility that some infections may be caused by organisms which are intermediate in their agglutinin producing properties between the frankly epidemic and the frankly murine types.]

John W D Megaw

HERRERA J R. Informe sobre tifo exantemático ocurrido en la ciudad de Guatemala durante el mes de abril de 1944 [Report on an Outbreak of Typhus Fever in the City of Guatemala in April, 1944] *Bol Oficina Sanitaria Panamericana* 1944 July v 23 No 7 603-7 1 fig English summary

This outbreak occurred in The Home for the Insane of Guatemala its chief interest lies in the fact that about 88 cases with 25 deaths had occurred during the month preceding the date on which the existence of a communicable disease in the institution was notified to the health authorities Control measures on orthodox lines were carried out with energy and in less than a month the epidemic came to an end.

During the month of April after the notification of the disease there were 198 proved cases with 63 deaths in the home and 30 cases were detected elsewhere in the City

John W D Megaw

PATÍÑO-CAMARGO L. Tifo exantemático en Colombia. [Typhus in Colombia] *Bol Oficina Sanitaria Panamericana* 1944 Aug v 23 No 8 675-6 English summary

Of 1,319 cases of typhus reported in Colombia 752 were reported from the hospitals of Bogotá (303 women 482 men 51 deaths mortality 6.64%) There were cases in 34 municipalities of Antioquia 6 municipalities of Boyacá 2 of Cauca, 7 of Caldas 18 of Cundinamarca (including Bogotá) 9 of Narino 2 of Santander and 1 of Tolima. Verification was made by isolation of the virus from blood of patients inoculated into guinea pigs through finding of

Rickettsia and by agglutination with *Proteus*. No spotted fever was verified during the year 1943. [Elsewhere the figures are given as women 282, men 460. This total appears to be correct.—Ed.]

AVRIAN A. P. [The Pathology of Exanthematic Typhus.] *Alimicheskaya Medicina* Moscow 1944 v 22 No 4 44-52. [17 refs.] [In Russian.]

When mice are inoculated intranasally with suspensions of rickettsia a specific bronchopneumonia is produced which passes through the following stages—(1) after one hour swelling of alveolar epithelium some desquamation, with single rickettsiae in the cast-off cells. (2) 12-18 hours vascular reaction, diffuse hyperaemia of lungs rickettsiae present in the alveolar epithelium. (3) 24-48 hours formation of foci of bronchopneumonia. (4) 60-90 hours extensive consolidation necrotic foci surrounded by haemorrhagic areas. Many rickettsiae present, in bronchial and vascular endothelium, and also in giant cells not seen in lymph nodes nor in smooth muscle fibres of bronchi and blood vessels. In the early stages bodies resembling droplets were seen in the bronchial and alveolar epithelium, having the same staining reactions as rickettsiae. These can, however be scarcely considered as initial bodies, as they were also seen in the liver where rickettsiae were not found, and also in the bronchial epithelium of mice with streptococcal pneumonia. It is suggested that they represent a cellular reaction to the presence of the parasite. The effect of rickettsial endotoxin was observed by injecting mice intranasally with a massive dose of virulent lung suspension. Death occurred in 24 hours with hyperaemia of the lungs and haemorrhages. D J Bauer

WILCKENS H. Zur Klinik des Fleckfiebers. [Clinical Aspects of Typhus Fever.] *Med Klin* 1943 Oct. 1 v 39 No 39/40 671-4. [14 refs.]

These notes are based on the observation of 315 cases, mostly very severe of typhus fever seen in the months of January February and March, 1943 in a Field Hospital in the "Middle East". There were 40 deaths.

The patients were inclined to be somnolent by day and excited by night. When the wards were brightly lighted at night this inversion of the day and night rhythm became less pronounced. More than two-thirds of the deaths occurred before the end of the febrile period. Twelve patients who had been inoculated suffered from exceptionally mild attacks, but several patients whose illness began before the third dose of vaccine was given had attacks of average severity. A high-intermittent type of fever curve was usual in cases with pneumonia or septic complications. An "after fever" lasting 1-2 days was often seen shortly after desferescence. The author believed that a rickettsial endotoxin played a more important part in the early stages of the illness than the arterial lesions. In one patient who died on the 5th day very few typhus nodules were found in the brain. An unusual complication was diphtheria which occurred in 14 cases, and was regarded as the cause of death of five patients.

Septic complications there seemed to be no failure in the development of immunity to the secondary infection. Healing was surprisingly satisfactory.

In a considerable number of cases a fine powdery desquamation was seen on the face for some time after desferescence though the typhus rash had not been tested on the face in any of the patients. There were no cases of gangrene, eschara sores were rare and when they did occur they yielded readily to treatment. The lunulae of the nails were observed to assume the same colour as the rest of the nails early in the course of the fever. The urine contained cylindrical casts and small quantities of albumin in all cases.

No great claims are made for any kind of drug treatment. Calcium gluconate and atabrin were tried at the beginning of the epidemic, but the author formed

the opinion that luminal gave better results. He gave this drug in doses of 0.03 gramme five times daily and also a single dose of 0.2 gramme every evening. Strophanthin was given intravenously every two days and sympatol was injected subcutaneously every two hours.

Convalescence was very slow a period of at least 4-6 months was found to be essential.

John W D Megaw

LAURE G. Remarques cliniques et thérapeutiques sur les gangrènes du typhus
[Clinical and Therapeutic Observations on Gangrene in Typhus Fever]
Bull Inst Hyg Maroc. 1943 v 3 59-86 2 pls

The author saw 120 cases of gangrene among 2014 typhus patients in French Morocco during the year 1942. He classifies the disease in two groups one of which the common type is called distal the other in which a considerable part of one or both limbs is affected is called global. In both types the gangrene is usually dry being caused by a purely arterial lesion but in some cases the veins also are affected and there is a combination of dry and moist gangrene. The global type tends to occur early in the course of the fever the distal type appears late in the illness often during convalescence.

Few females were attacked no case was seen among Jewish patients and among 50 European patients there were only three cases. In nearly all the cases the disease was restricted to the lower extremities.

Distal gangrene which usually affects both limbs is described as being of three degrees of severity. (a) the least severe appearing most commonly in early convalescence. The first symptom is pain in the tips of the toes which later become pale and cold and soon take on a livid hue. By the end of 4-6 days a superficial patch of dry gangrene appears on the distal and plantar aspect of one or more of the toes. The great toe is affected more often than the others. Spontaneous cure with the separation of a small slough is usual. (b) The average type sometimes occurs as an extension of type (a) sometimes the greater part of the toes is affected from the beginning the gangrene may extend as far as the metatarso-phalangeal joint. In all cases the deeper tissues are involved. The line of demarcation becomes sharp 10-15 days after the onset and a natural amputation soon follows. (c) The severe type which may be an extension of type (b) or may set in with rapid involvement of the whole or greater part of the foot.

Global gangrene is usually bilateral. The onset tends to be sudden half or two-thirds of one or both legs becomes cold painful and cyanosed, almost simultaneously. The popliteal pulse is imperceptible and the femoral pulse is feeble. Mummification is apparent within 4-5 days. Occasionally the condition is a gradual extension of the severest form of distal gangrene.

Moist gangrene is usually a complication of the dry form, it usually starts above the line of demarcation but occasionally the gangrene is moist from the outset.

The treatment specially recommended is blocking of the lumbar sympathetic ganglion by infiltration with 10-20 cc. of 1-200 solution of novocain without adrenaline. The needle is inserted at a point four fingers breadth from the tip of the spinous process of the 2nd lumbar vertebra [presumably measured on a horizontal line] and is inclined at an angle of 60° till it touches the vertebral column, when the needle is brought to a vertical position and is made to follow the plane of the bone till the end of its travel. [These instructions cannot be regarded as a complete guide to a novice.] After a successful infiltration the limb immediately feels warm and if the treatment is started early the pain disappears or is greatly relieved after two injections. After four or five injections given daily the limb becomes warm and the slough becomes absorbed. It is

claimed that early treatment arrests the course of the disease, and that even at a later stage the relief of pain enables the surgeon to continue to "temporize and wait for a natural termination of the disease with its resultant economy in the loss of tissue. But the attitude of temporizing and economizing must not be adhered to in cases with secondary infections in these the result may be a greater risk to life and if recovery occurs the final loss of tissue may be much greater

John W D Mcgaw

LEMAIRE G Contribution à l'étude des effets du vaccin de G BLANC. Vaccination massive d'un foyer épidémique. Expérience de la Casbah. Difficultés d'interprétation des statistiques relatives aux milieux indigènes. [A Contribution to the Study of the Effects of Blanc's Vaccine.] *Bull Soc Path Exot* 1943 July 7 v 38 Nos 7-8 202-7

The new type of Blanc's living vaccine has the great advantage of keeping for an indefinite period when stocked in dry form *in vacuo*

About 35 000 persons, constituting 70 per cent. of the population of the quarter were inoculated in the Casbah section of Algiers within seven days in February 1942 during an epidemic.

Carefully controlled observation of the results was made, starting 37 days after the completion of the inoculation so as to allow for the maximum incubation period of 27 days (for inoculated murine typhus) and an extra margin of 10 days for any possible extension of this period

From March 20th to August 1st there were 121 cases with four deaths among 35 000 inoculated persons and 422 cases with 73 deaths among 15,000 non-inoculated persons.

The case incidence was, therefore 8 times higher among the unprotected than among the protected, and the case-fatality rate was $\frac{1}{10}$ th higher in the former than in the latter group

BLANC is quoted as stating that about 40 per cent. of the vaccinated are not immunized.

A striking finding was that among 19 vaccinated patients aged 41 years and upwards there was no death whereas among 94 non-vaccinated patients belonging to the same age group there were 40 deaths

John W D Mcgaw

LEVKOVICH E. \ [Active Immunisation against European Spotted Fever. Communication I. Adaptation of the Virus of the European Spotted Typhus to the Organism of White Mice.] *Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii* Moscow 1943 No 1-2, 33-8 [In Russian]

— & PETRISHCHEVA, P A [Communication II. Comparative Valuation of the Effectiveness of Spotted-Typhus Vaccines in Experiments on Animals and in Epidemiological Tests on Man.] *Ibid* 38-43 [In Russian] [Summary taken from *Rev Applied Entom* Ser B. 1944 Dec v 32, Pt 12, 218-19]

DURAND & SPARROW found that prolific multiplication of the rickettsiae of *Marseilles* fever or murine or epidemic typhus took place in the lungs of white mice that had been infected intranasally and DURAND & GIROUD successfully used such infected lungs for the preparation of typhus vaccine. These results were confirmed by the experiments described in the first paper in which characteristic pneumonia infection with a large accumulation of *Rickettsia prowazekii* was produced in white mice by intranasal injection of a centrifuged emulsion of the intestines of bee (*Pedicularis montana* L.) that had fed on typhus patients and was subsequently maintained in further mice by similar injection of lung-tissue emulsion. The virulence of the infection was increased by serial passage.

In the second paper the results are given of tests on guineapigs and man of the protection against epidemic typhus afforded by Cox's vaccine (prepared from *R. prowazeki* cultivated in the tissue of the yoke sac of a chick embryo) a vaccine made from infected mouse lung and vaccines prepared by two slightly different methods from the intestines or whole bodies of infected lice. All were efficient and there was no evidence that one was preferable to another except that the vaccine prepared from the whole bodies of lice was less satisfactory, as it caused an allergic skin reaction in two instances.

Details are given of the method adopted for rearing the lice in large numbers in order to obtain vaccine from them. They were kept at 30–32°C. [86–89.6°F] and 85–90 per cent humidity in small wooden boxes (4 × 2½ × 10 cm) with tightly fitting lids and with bottoms of bolting silk. A piece of muslin folded double was placed over the lice in each container which would hold 100–150 large adults or twice as many larvae. The lice were allowed to feed for an hour twice daily by strapping the boxes round the hips of women who were immune from typhus. Uninfected lice were not fed on the same woman as infected ones so that they could not become infected by feeding on the excreta of the latter. Feeding once daily instead of twice reduced the numbers of eggs laid per female from 230–300 to 160–200 and resulted in high mortality of the young lice which became too weak to suck blood if starved for 15–20 hours after hatching.

The lice usually settled and oviposited on the muslin that covered them. The muslin was renewed weekly when the boxes were cleaned and the old pieces with the eggs were put in fresh ones. Under the conditions of rearing the rate of mortality was only 2–10 per cent in the egg stage and 25–35 per cent during subsequent development and the life-cycle averaged 19 days. The eggs hatched in 6–7 days. The extremes of temperature at which hatching occurred were 22–23 and 38°C [71.6–73.4 and 100.4°F] practically all newly laid eggs lost their viability in 3–5 days at temperatures below 23°C.

The lice were infected by Weigl's method of rectal injection or by feeding them on typhus patients during the first 4–6 days of illness the latter method resulting in the infection of about 50 per cent. They were given three or four feeds of an hour's duration on the typhus patients in the course of two or three days and were then fed on healthy women as before since if they were fed on a patient after the sixth day of illness the rickettsiae did not accumulate in them and frequently did not develop at all being apparently neutralised by the substances that appeared in the patient's blood. A third method of infecting lice developed by PSHENICHNOV but not used by the authors consists in allowing them to feed on the skin of an immune person after it has been smeared with an emulsion of infective material. The temperature and humidity at which the lice were normally reared proved most favourable for the development of rickettsiae in them. The rickettsiae appeared and attained their maximum numbers 5–7 and 14–16 days respectively after the lice were fed on the patients.

PSHENICHNOV A. V. [A Universal Method for studying Infections transmitted to Man by Blood-sucking Insects and a New Vaccine against Spotted Typhus] *Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii* Moscow 1943 No 1–2 43–8 [Summary taken from *Rev. Applied Entom.* Ser. B 1944 Dec. v 32 Pt 12 219–20]

The author and his collaborators have devised a method of infecting lice [*Pediculus humanus* L.] with typhus in large numbers by allowing them to feed through a piece of animal membrane on defibrinated human blood to which has been added an emulsion of infected louse intestine or guineapig brain. The appearance of *Rickettsia prowazeki* in the lice usually occurred after 7–9

[April, 1945]

days. The blood is warmed to about the temperature of the human body and is kept at slight pressure under the membrane. This method of feeding has also been successfully used by Mitrofanova to infect lice with bacteria and preliminary work has shown that other blood-sucking insects and even ticks will take blood through membranes.

The advantages of infecting the lice in this way over Weigl's method of rectal injection include the avoidance of injury to the lice the ease with which large numbers can be infected and the fact that immature lice as well as adults can be used. A typhus vaccine as effective as that of Weigl was prepared from third-instar lice that had received their infecting feed when they were newly hatched and were then fed once a day on man for 9-10 days. Weigl's vaccine can only be obtained by feeding lice on man twice a day for about a month.

In preliminary experiments lice were reared from eggs to adult when fed exclusively through membranes. In this case titrated blood proved better than defibrinated blood. In comparison with lice fed on man however the duration of development was rather longer the rate of mortality during moulting was higher and the surviving females laid fewer viable eggs.

RAIKOVA, B. L. (Fundamental Principles of the Technique of preparing Vaccine against Spotted Typhus from Intestines of Lice by Pahlenkova-Halcher's Method.) *Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii*, Moscow 1943 No. 1-2, 43-51. [Summary taken from *Rev. Applied Entomol.* Ser. B 1944 Dec. v 32, Pt. 12, 220.]

Details are given of the technique used to prepare a typhus vaccine from the third instar lice (*Pediculus humanus* L.) infected in the first instar by feeding through a membrane (see preceding paper) with notes on the method of feeding lice and of obtaining a constant daily supply of them. For the latter purpose adults were kept at 30°C (86°F) and a relative humidity of 70-80 per cent. in glass jars containing chopped human hair and were allowed to feed on man for 30 minutes twice a day. A ratio of one male to four females secured maximum oviposition and hatching of 98-4 per cent. of the eggs. The hairs with the eggs on them were daily transferred to other jars and hatched in about five days. The newly hatched lice were collected by allowing them to crawl on to small pieces of fabric that had been rubbed against human skin, to which they were attracted by the odour of perspiration.

The infective blood on which the lice were fed was in a small metal box over which a membrane was stretched and held in position by means of a ring. They attached themselves quickly when scattered over the membrane and completed their feed in 15-120 minutes the time varying with the quality of the membrane employed. Up to 1,500 could be infected simultaneously on each feeding box and the blood in a box remained infective for at least 24 hours. After infection they were fed on man once a day. More frequent feeding did not affect the time of appearance or the intensity of the development of the rickettsiae though it somewhat reduced the rate of mortality among the lice. With one daily feed however the rate of mortality did not exceed 30 per cent. during the 10-14 days required for the appearance of the rickettsiae.

SUMNER, Edm. & BÉGUER, M. Conclusions pratiques à tirer d'une expérience d'épouillage par poudrage insecticide faite à Maison-Carrée et à Arba (Algérie). [Practical Conclusions drawn from an Experiment in Delousing by Insecticidal Dust.] *Arch. Inst. Pasteur d'Algérie* 1944 June v 22, No 2, 108-112.

This is a preliminary account of practical trials of dust insecticides for delousing carried out in collaboration by Dr G. K. SUMNER and other doctors

of the Rockefeller Foundation and workers of the Pasteur Institute of Algiers. Two dusts were used. MYL [pyrethrins iso-butyl undecyleneamide and dinitro anisole] and DDT [probably at 10 per cent]. The trials were made (1) on the prisoners at the Maison-Carrée penitentiary (2) on the villagers at Arba, 30 km from Algiers.

It was found that one dusting with the DDT dust or two treatments with MYL formula effectively rid a person of lice. It was possible to do the dusting without undressing the people by using dust guns to blow the powder under the clothes. For this reason and the innocuous and effective characters of the dusts these treatments were quite popular among the people treated.

Reinfestation eventually occurred because it is impossible completely to segregate any community even of prisoners. It is considered to be impossible to rid a district of lice even by treating hundreds of thousands of people because the lice would finally spread again. The great value of these dusts would be best employed by a mobile disinfecting unit to check typhus outbreaks.

J R Busvine

HARRINGTON C & YOUNG E A E. Murine Typhus in the District of Port Elizabeth, South African Med J 1944 Nov 11 v 18 No 21 368-9

Murine typhus infection has already been detected among rats in many parts of South Africa.

The authors have now isolated murine rickettsiae from rats in the Cape Eastern Province at a place about 25 miles from Port Elizabeth and also from a patient on whose farm the rats were caught. It is mentioned that one of the 10 cases of typhus-like fever described by SCROGGIE and GRAY in 1931 occurred in the same locality in these ten cases louse transmission was regarded as being excluded but rats and their fleas could not be incriminated.

The present patient had an attack of typhus fever lasting 20 days the agglutination titre with *Proteus OX19* was 1-800 on the 9th day and 1-6400 on the 12th day. The reactions with *OX2* and *OXK* were negative. Two similar and cross-immunizing strains of orchitic rickettsiae were isolated and passaged at least 20 times through guinea-pigs. One strain was obtained from the patient's blood, taken on the 9th day the other from a pooled suspension of the brains of five rats (*Rattus rattus*) caught on the premises.

Both strains showed cross protection when tested on guinea-pigs against a murine strain isolated from rats at Paarl in the Cape Western Province by RHODES in 1934 and also against the Ettie epidemic strain isolated by GEAR from a patient during an epidemic of louse typhus in the Eastern Transvaal in 1939.

The responses of guinea-pigs and Cape gerbils to the two strains corresponded closely in those described by GEAR and DAVIS for South African murine strains.

John W D Megaw

ALICATA J E & BREAKS Virginia. Typhus Fever in Honolulu. Certain Epidemiological Aspects. Hawaii Med J 1942 Nov-Dec. v 2 No 2 59-62 3 figs.

An account is given of a careful survey of the incidence of murine rickettsial infection among the rats of Honolulu where 202 human cases of murine typhus have been notified during the five-year period 1937-1941.

In May 1941 a strain of rickettsia immunologically identical with the Wilmington murine strain was isolated from a patient. Rats were trapped in seven districts of Honolulu—100 in each of five districts and 50 in each of the other two. Brain suspensions from these were injected intraperitoneally

into 249 guinea pigs each animal receiving a pooled suspension from the brains of two or three rats. From 73 of the guinea pigs strains of rickettsiae identical with the above were isolated, so that at least as many of the 600 rats must have been infected a rate of 12.1 per cent.

Among 17 rats from premises in which typhus patients lived, infection was found in eight (47 per cent).

Human infection must have been acquired chiefly in the homes of the patients rather than in their places of work because among the 43 patients who had seen rats at their homes or places of work only four had seen the rats at their places of work and not at their homes. Seven other patients had not seen rats at either place.

The brains of 109 cats and 28 dogs from the area were examined with negative results. Fleas collected from six cats and one dog in houses where human infection had occurred recently were also negative.

The percentage incidence of rat infection in the seven districts was as follows (the figures in parentheses show the percentage of the 200 human cases that occurred in each of the corresponding districts) — 19 (16.7) 8 (2.9) 21 (12.8) 9 (4.9) 3 (3.4) 14 (28.7) 8 (2.9)

John W D Merges

RUIZ SÁNCHEZ F. Estudios sobre el tifo de Guadalajara. Anuario de un virus del tipo murino. [Studies in Typhus Fever in Guadalajara (Mexico) Isolation of a Murine Strain.] *Medicina Mexico* 1944 Sept 25 v 24 No 468 363-70 3 figs.

During the 12 years since 1932 when typhus fever was first recognized in Guadalajara, 182 cases have been notified. The seasonal distribution of the disease is remarkably uniform the cases occur sporadically all social grades of the community are equally affected lice are rarely detected on the patients rats and their fleas are abundant on the affected premises and the disease is rarely fatal.

The author has now isolated an orchitic strain of rickettsia from a patient also from the brains of rats caught in the same locality and from fleas collected from the rats.

He concludes that the typhus fever which is endemic in Guadalajara is of the murine flea-borne type.

John W D Merges

FARMER D S & KATSAMPES C P Tsutsumgamushi Disease. *U.S. Nav. Med. Bull.* 1944 Oct v 43 No 4 800-836 1 fig [201 refs]

[An adequate summary cannot be made of this paper which in itself is an admirable summary of what is known and believed with regard to the mite-borne tsutsumgamushi disease now often called scrub typhus.]

The authors define the disease as one of the typhus group of diseases caused by *Rickettsia tsutsumgamushi* transmitted by the bite of a larval trombiculid mite. They provisionally assume that the fever is primarily a widespread disease of several (or many) species of vertebrates in Asia and Australasia. The vector mite never feeds more than once on an animal host and therefore cannot transmit infection by its own bite but the offspring of the infected mite may acquire infection through the ovum and so be able to transmit the disease on the one occasion on which they bite.

The paper contains a fully documented account of the long and confused history of the disease which was first described by a Chinese writer in the 3rd century A.D. and was attributed by him to the bite of a minute red insect

presumably a mite. For many years the people of certain riverine areas in Japan have known the existence of the disease and have regarded it as being caused by the bite of a mite which they call *akamushi*.

In the section on the reservoir hosts it is stated that final proof of the transmission cycle has been established on only one occasion when the rickettsia was isolated from a field vole *Microtus montebelloi* and also from the mite *Trombicula akamushi* which was found capable of transmitting infection from the vole to man.

The bibliography contains references to 201 articles consulted in the preparation of the paper. These articles have been selected from a list several times longer. Although the paper is not lengthy it is so closely packed with information that it really constitutes a monograph on the basic aspects of the disease. Room has been found for many explanatory and critical comments which add greatly to the value of the paper. A useful feature is a glossary with explanations of more than 50 of the names that have been applied to the disease and this lengthy list is said to be by no means complete. The existence of so many names is an index of the confusion that has surrounded the disease up to recent times. This confusion is at first sight surprising because the disease appears to be strictly unitary, being caused by one species of rickettsia and transmitted by closely related species of mites. The chief misunderstanding has been due to the fact that the occurrence of a local sore and associated adenopathy was long regarded as an essential feature of the classical tsutsugamushi disease so that the absence of local lesions was considered to rule out the diagnosis of this fever.

[It is interesting to find that 24 of the synonyms of the disease include a reference to the arthropod vector and 16 contain the word typhus so it seems fair to suggest that the name mite typhus which combines a reference to the vector and the clinical type of the disease has decided advantages.]

The authors point out that the disease described by SCHÜFFNER in 1910 as pseudotyphus ought to be called pseudotiphoid in English as was done by Schüffner himself in his papers in English on the disease. Many authors fail to realize that what the Germans call [abdominal] typhus is called typhoid by writers in English.

Only one trifling error has been noticed in the paper. The authors state that the name mite typhus was proposed as being parallel to flea typhus (endemic typhus), louse typhus and tick typhus but the existence of flea typhus was not known till several years after 1921 when the reviewer suggested the names mite typhus, louse typhus and tick typhus. He later suggested the name flea typhus as being more suitable than murine or endemic typhus.

The description of the geographical distribution of the disease is admittedly based on the assumption that an OXK type of agglutination response is reliable evidence that a case of fever is tsutsugamushi disease. The authors appear to accept this assumption though they point out that the agglutination of OXK by the serum of animals is not sufficient evidence that these animals are infected by *R. tsutsugamushi*. They also quote an example of the isolation of *Proteus* OXA from an animal in which this type of response occurred. The OXA reaction is invaluable as an aid to diagnosis but the question still remains whether it can be relied on for the identification of mite-borne typhus in circumstances in which there is no other evidence of the existence of this disease.

[Research workers on the typhus fevers will be specially grateful to the authors who at the cost of great labour have provided an admirable work of reference on the basic problems connected with mite borne typhus. But the paper ought also to be read by every medical man working in the East and particularly by medical officers serving in areas in which the disease is of major military importance.]

John W. D. Megaw

LOGUE, J B Scrub Typhus. Report of Epidemic in the Southwest Pacific. U.S. War Med Bull. 1944 Oct. v 43 No. 4 645-9 1 chart

This is a brief account of an outbreak of mite-borne typhus in an island in the South-West Pacific area. Among an unstated number of U.S.A. troops there were 230 cases and 22 deaths within a period of less than four months. The troops landed on December 23rd, 1943 and the first case occurred four days later. Within a month the peak period of incidence was reached. 33 cases occurred during the week ending February 5th. Then a steady decline set in, and there were only three cases during the first week of April. The troops departed from the island on April 30th, having had no fresh cases during the previous 17 days.

The troops were working and bivouacking on wet ground covered with kumal grass growing to a height of 10-20 feet. The preventive measures, which proved effective were — (1) Selection of well drained camps whose sites had been burned down beforehand when this was possible. (2) Sometimes the only practicable preparation of the site consisted in the removal of grass, shrubs, leaves and rubbish, from the sites and paths. (3) Tent sites and paths were sprayed with thin oil, and orders were given to the men to keep to the prepared paths, and to avoid sitting down on the ground. (4) Rat control was applied to the legs and worked well into the clothing from the waist to the feet. Insecticide powder was applied round the waist and ankles also inside the boots and leggings. After excursions into infested areas, the clothing was removed, and the whole body except the genitalia, was lightly rubbed with a cloth moistened with kerosene then clean clothing was put on.

The incubation period was 4-18 days. The typical eschar and regional adenopathy were usually present. Apart from the occurrence of these and of "relative leucopenia" the clinical features of the disease do not seem to have differed in any essential respect from those of louse-borne typhus. The treatment was supportive, by intravenous fluids, plasma and small transfusions of blood. Oxygen was very prolonged. weakness and palpitation persisted after several months of rest and it was suspected that permanent myocardial damage might result from the disease.

The mortality rate is said to have been higher among Japanese troops exposed to similar conditions.

Certain damp coastal areas were found to be specially dangerous high-lying and well-drained ground was relatively safe even when covered with the same kind of grass.

John W. D. Megeath

КОЗДЕНКОВА О. С. Etiology of Tick Spotted Typhus in Krasnoyarsk Province. Zhurnal Mikrobiologii, Epidemiologii i Immunologii. Moscow 1943 No. 1-2, 59-64 7 graphs. [In Russian.]
КРОТОВСКАЯ, М. К. & СЕДАТКОВ, М. Д. [On the Epidemiology of the Tick Spotted Typhus of Central Siberia. Ibid 65-8. [In Russian.]]
БОЧАРОВА, Т. В. On the Epidemiology of the Tick Spotted Typhus. Ibid 68-72, 1 graph. [In Russian.]
[Summary taken from Rev. Applied Entom. Ser. B 1944 Dec. v 32, Pt. 12, 220-21.]

In the first paper an account is given of investigations on the causal agent of a disease transmitted by *Dermacentor nuttalli* Olen. epidemics of which occur in spring and summer in the Province of Krasnoyarsk (central Siberia). It called tick-typhus, since its symptoms were similar to those of epidemic typh. It proved to be pathogenic to guinea-pigs, rabbits and monkeys, but not

white rats *Rickettsiae* were observed in the tunica exudate of the guineapigs and the rabbits and monkeys gave a positive Weil Felix reaction which was most marked with *Proteus* O\19. Cross immunity tests demonstrated the identity of the strains of the causal agent isolated from different patients from examples of *D. nuttalli* collected in a focus of the disease and from ground squirrels [*Citellus*]. A strain from man immunised guineapigs against Marseilles fever but not against a guineapig strain of epidemic typhus. On the other hand the last strain conferred almost complete immunity from the tick typhus strain while Marseilles fever conferred none.

Much of the information in the second paper is similar to that already noticed. Investigations in central Siberia revealed a focus of tick typhus of three years standing in a steppe district where *D. nuttalli* was practically the only tick found. It occurred in areas overgrown with grasses the adults were abundant on cattle and numerous larvae were taken early in July on *Citellus evermanni* and *Stenocranius* (*Microtus*) *gregalis*. The other ticks found were *D. silvarum* Olen. and *Ixodes persulcatus* Schulze but they occurred in negligible numbers and *I. persulcatus* was confined to places covered with woody vegetation where the adults were taken on cattle horses dogs and cats. Natural infection was found to be prevalent in *D. nuttalli* and guineapigs contracted the disease when the ticks were fed on them. Possible measures for the control of ticks are discussed. They include the burning or mowing of grass the application of sprays the dipping of cattle and measures directed against the rodent hosts.

In the third paper is recorded the finding of several foci of tick typhus in eastern Siberia where areas overgrown with low woody vegetation or tall and dense grass provided favourable conditions for ticks and rodents. All the infected persons had been bitten by ticks and the numbers of cases were greatest in localities in which ticks were most abundant. Natural infection was demonstrated in *Eutamias asiaticus* *Criceolus furunculus* *Microtus michnoi* *Apodemus agrarius* and the house rat *Mus* (*Rattus*) *norvegicus* and also in a large proportion of larvae of ticks on rodents and of adults on cows and dogs. The infection in larvae suggests that the causal agent persists in ticks from one generation to the next and this view is supported by experiments by workers in central Siberia in which guineapigs were infected by inoculation of eggs laid by ticks taken in the field, and also by the bites of the larvae and nymphs of ticks including *D. nuttalli* *D. silvarum* and *Haemaphysalis concinna* Koch. Suggestions similar to those in the second paper are made for tick control.

YELLOW FEVER.

AFRIQUE OCCIDENTALE FRANÇAISE RAPPORT SUR LE FONCTIONNEMENT
TECHNIQUE DE L'INSTITUT PASTEUR EN 1942 (DURIRUX C.) pp 53-69
Service de la fièvre jaune [Yellow Fever Service.]

The preparation of yellow fever vaccine follows the methods previously described [see this *Bulletin* 1940 v 37 92 and 1942, v 39 761]. The virus employed had undergone 255 to 257 passages in mouse brain and its characters had not varied during the period under consideration. During 1942 a total of 3,238,500 doses of yellow fever vaccine had been prepared and in addition 33 680 ampoules of 2 per cent. gum arabic for use in making suspensions of the dried vaccine. It is recommended that any vaccine not used within half an

hour of preparing the suspension should be rejected. Nevertheless, the vaccine is evidently able to withstand considerable vicissitudes for a consignment that had been broken en route was examined for virulence after being at temperatures of 30°C and over for at least six weeks under unfavourable conditions and the virus killed two out of three mice in dilutions of 1:1,000,000.

A total of 2,913,114 persons were inoculated either subcutaneously or by scarification during the year and it is estimated that by the end of 1942 a third of the total population of French West Africa had been vaccinated against yellow fever. The results of protection tests with the sera of vaccinated persons showed that after less than one year 2,207 out of 2,305 were positive after one year 49 positive out of 49 and after two years 10 positive out of 10 examined.

The pathological anatomy department examined the livers of 34 persons suspected of dying of yellow fever of these nine were positive. The following rapid method of preparing tissues described by POURRIERES and DEZERT (*Médecine Tropicale* 1942, No. 2, p. 120) has been adopted, as sections can be prepared within 150 minutes.

Tissues from cadavers are sent to the laboratory in 5 per cent. formalin. They are then cut into pieces 1 mm. thick and fixed in Duboscq Brazil, alcoholic picro-formol [picric acid 1 gm. formol 60 cc. glacial acetic acid 15 cc. 80 per cent. alcohol 150 cc.] at 56°C for 15 minutes passed through seven changes of alcohol each of 5 minutes at 37°C passed through seven similar changes of xylol at 37°C. finally passed through three baths of paraffin wax each of 10 minutes. The blocks are then cut and the sections fastened on to the slides by means of gelatin (16 minutes) and then stained with haematein-coum. safranin.

During the year 10 cases of yellow fever (nine fatal) were diagnosed, including seven Europeans and three Africans. Details are given of eight of these cases. The patients all lived in sparsely populated areas and with one exception there was no relation between the various cases either in time or locality. The epidemiological evidence supports the view that at least 6 of these cases were probably examples of jungle yellow fever. Six of the ten had not been vaccinated against yellow fever two had been vaccinated some time previously in the remaining two both Africans it was uncertain whether they had been vaccinated or not.

The cause of these occasional failures to develop immunity after vaccination is discussed and it is considered that they may be due to the vaccine being rubbed off before the virus has had time to pass through the cutaneous scarifications. In order to avoid this possibility the vaccine, after being deposited on the skin is kept under observation until it dries when the contained gum arabic forms a protective covering.

E. Hindle

ELLIOTT M. Yellow Fever in the recently Inoculated. *Trans Roy Soc Trop Med & Hyg* 1944 Dec v 38 No. 3 231-4 1 chart.

The author gives details of three cases of yellow fever which came under his care and are of interest since at that time (June 1942) they were the only cases that had occurred among British and Allied troops since the beginning of the war.

All three men had received preventive inoculation at least two years earlier. In two cases there was a severe clinical course and rapid onset of death, suggesting that the initial immunity against yellow fever was slight. All three developed the disease in West Africa.

It is noted that at least 135,000 people received preventive inoculation between January 1941 and June 1942, therefore the prophylactic value of the

anti yellow fever inoculations has been proved beyond question and the catastrophic annihilation of large numbers of white troops may have been prevented

E Hindle

DE ASSUMPTÃO L. Relações imunitárias entre febre amarela e outras infecções clinicamente parecidas que se observam nos climas tropicais e subtropicais [Immunity Relations between Yellow Fever and Diseases resembling it Clinically in the Tropics and Subtropics.] *Arquivos de Hig e Saúde Pública* São Paulo 1944 Sept, v 9 No 22 19-32 [22 refs]

The author first gathers together the evidence which shows that the viruses of urban rural and jungle yellow fever are identical, and that laboratory animals immunized against one are immune to the others. He then takes up the question of dengue Rift Valley and sandfly fevers as a group of diseases which may be confused with yellow fever. As regards *dengue* he quotes Jorge as saying that the similarities are more apparent than real [whatever that may mean]. It seems strange that anyone acquainted with both dengue and yellow fever would ever confuse them. Anyway the protective test and absence of cross-immunity would soon set the matter at rest. Next *Rift Valley fever* animals such as cattle sheep goats susceptible to Rift Valley fever are not susceptible to yellow fever and there is no cross immunity between the two diseases. The author quotes the case reported by FINDLAY and MACCALLUM of a laboratory assistant who had an attack of yellow fever in 1931 and of Rift Valley fever in 1934 both viruses being isolated from his blood. The similarities between the two diseases are certainly striking in man. Clinically the symptoms of the former are like those of yellow fever both produce liver necrosis with intranuclear inclusions and Councilman lesions both give rise to lasting immunity and both are transmitted by *Aedes*. But there is no true cross-immunity between them though the *interference phenomenon* may be seen as FINDLAY and MACCALLUM [this *Bulletin* 1937 v 34 689] have demonstrated. Of 10 *Macacus rhesus* inoculated with the two pantropic viruses intraperitoneally or subcutaneously seven were protected camondongos inoculated with neurotropic yellow fever virus and with pantropic Rift Valley virus lived longer than after inoculation with either singly and some might survive but no protection is afforded if the Rift Valley fever virus is inoculated 24 hours before the yellow fever virus.

Though an attack of *sandfly fever* imparts a certain degree of immunity against a second attack in the succeeding season, this immunity is not lasting and there is no cross immunity between it and yellow fever.

Lastly *spirochaetal jaundice* may be confused clinically with yellow fever [as the classical studies of NOGUCHI proved] but laboratory tests—finding of the *Leptospira* in the blood or the urine agglutination results and animal inoculation—will suffice to differentiate and there is no cross immunization with yellow fever virus.

H Harold Scott

LINHARES H. Inoculação do vírus amarelo em gatos jovens [Inoculation of Yellow Fever Virus in Kittens.] *Mem Inst Oswaldo Cruz* 1943 Apr v 38 No 2 201-7 English summary

1 Young cats inoculated intracerebrally with relatively large doses of neurotropic or viscerotropic virus and intraperitoneally with viscerotropic virus fail to show circulating virus up to 12 days post inoculation.

2. Such cats also fail to show symptoms referable to the virus.

3 It was impossible to isolate virus from the brains of inoculated cats dying in the course of the experiments and histological examinations of the brains failed to show encephalitis (only one case with toxic encephalitis).

"4. The development of serological immunity after 30 days was observed in all but two of the cats inoculated intracerebrally or intraperitoneally with neurotropic virus with Asibi strains, only two positive results were obtained by the intracerebral route

"5 Young cats are relatively insusceptible to yellow fever virus, only giving the reaction of immunity "

LIXHARTS, H. Suscetibilidade de camundongos ao virus amarelo administrado por vias extraneuras. [Susceptibility of Mice to Yellow Fever Virus administered Extranurally.] *Mém. Inst. Oswaldo Cruz* 1943 Apr v 38, No 2, 209-24 [10 refs.] English summary

"1 French neurotropic Asibi and vaccine (17D) virus infect young mice (21 days) when instilled in the nostrils killing them with symptoms of encephalitis, or developing immunity

"2 French neurotropic virus and Asibi (and perhaps vaccine virus) when instilled in the ear of young mice may infect them, producing development of immunity

"3. After instillation in the scarified cornea of young mice French neurotropic virus, Asibi and perhaps vaccine virus, may produce infection. If the cornea, however is undamaged, it has not been found possible to infect mice in this way

"4 French neurotropic virus, Asibi vaccine Asibi Egg I and Egg III introduced into the stomach, may infect young mice causing a fatal encephalitis or rendering them immune.

"5. It is possible to infect mice 0-6 days old by simple deposition of virus or rubbing the suspension on the whole or scarified skin.

LIXHARTS, H. Suscetibilidade de pintos ao virus amarelo neurotrópico [Susceptibility of Chicks to Neurotropic Yellow Fever Virus.] *Mém. Inst. Oswaldo Cruz* 1943 Apr v 38 No 2 225-51 English summary

"1 After 80 serial passages from brain to brain of chicks, neurotropic virus fails to show essential modifications in the behaviour of the virus in mice or chicks.

"2 Chicks are susceptible by intracerebral, intraperitoneal and intradermal route, showing high levels of circulating virus and become immune when inoculated during the first days after birth. But circulating virus varies however in inverse ratio to age. It does not seem possible to infect chicks by the gastric route.

"3 During the first days virus may be found occasionally in the lungs, liver spleen and kidneys. Some days afterwards, no chicks showed virus in other organs than brains in which virus persists up to 10th day post-intraperitoneal inoculation and up to 15th day after the intracerebral inoculation, and perhaps till later. We have however not been able to isolate the virus from excretions

"4 There does not seem to be any difference in susceptibility to the yellow fever virus in chicks with B avitaminosis

"5. Detectable immune bodies appear 10-11 days after intraperitoneal and intracerebral inoculation at a time when many of the chicks still have virus in the brain.

"6. Age has a marked influence on the development of immunity in chicks inoculated by intraperitoneal route.

7 The multiplication and circulation of virus after intradermal inoculation of 50 to 160 M.L.D. renders possible the suggestion that infected mosquitoes can diffuse the virus among chicks and perhaps other birds a few days old.

LINHARES H. Transmissão de imunidade antiamarílica da mãe aos filhos em camondongos. [Transmission of Yellow Fever Immunity from Mother to Offspring in Camondongos.] *Mém Inst Oswaldo Cru.* 1943 Apr v 38 No 2 187-200 2 charts English summary

An interesting and important article recalling confirming and amplifying work of ten years ago which if not forgotten has at least tended to recede into the background. In 1934 HOSKINS [this *Bulletin* 1934 v 31 840] showed that yellow fever antibodies were transmissible in *Macacus* across the placenta and probably also via the milk and in the same year STEFANOPOULO [*ibid* 842] showed the same to hold good for camondongos and two years later STEFANOPOULO LAURENT and WASSERMANN proved that blood from the umbilical cord and also the milk of immune mothers contained protective antibodies [this *Bulletin* 1937 v 34 346].

In the present paper the author has by series of carefully planned experiments verified these results and demonstrated how early immunity is transmitted and for how long it persists. The camondongo is a good animal for experiment because it is easily reared in the laboratory it has fairly numerous progeny the gestation period is short growth of the young is rapid and they are easily handled.

Active immunization was performed by subcutaneous inoculation of the mother with 0.12 cc. of 15 per cent suspension of neurotropic virus of camondongos moribund from yellow fever encephalitis passive immunization by injection of hyperimmune Rhesus serum. Immunity in the mother was verified by intracerebral inoculation of 0.03 cc. of 2 per cent starch emulsion with 0.2 cc. intraperitoneal injection of 15 per cent suspension of neurotropic virus. In the offspring up to 17 days 0.01-0.32 cc. of the same virus subcutaneously was used those 21 days old received 0.03 cc. intraperitoneally those over 21 days old were inoculated in the same way as the mother. Abundant controls were used throughout the experiments.

The following sets of experiments were carried out. First the offspring of immune mothers were shown to be immune but no evidence was found to indicate that the virus passed either via the placenta or the milk consequently it follows that the immunity conferred is passive. Second by another series of experiments it was shown that antibodies traverse the placenta. Four females gave birth to young about 20 days after being inoculated with the virus and the young were taken away and suckled by non inoculated mothers who had just had young. Twenty-one out of 23 inoculated with virus survived whereas all but two of 22 normal young died. Thirdly females were inoculated with the virus on the day of parturition and suckled their offspring for 21 days at the end of that time the latter were found to be immune showing that antibodies had passed in the milk of the mothers and had been absorbed in the intestine of the young.

Next the author took two lots of females and to one lot virus was administered. Both lots parturated about 25 days later and the offspring of the immunized mothers were suckled by the non immunized and *vice versa*. Twenty-one days later 98.4 per cent (108 out of 112) of the normal offspring suckled by the immunized mothers were immune but only 10 per cent. (11 out of 109) of the offspring of the immunized mothers suckled by the unimmunized.

Further experiments showed that transplacental immunity was of brief duration diminishing rapidly after birth and disappearing altogether by the

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eleventh day. Also that immunity acquired through the milk is slight at first and increases up to the tenth day and animals so fed remain immune for another eleven days or if suckling is continued, as long as lactation lasts. Finally camoudongos passively immunized by injection of serum of hyper-immunized Rhesus monkeys transmit a temporary immunity to their offspring by way both of the placenta and of the milk.

H. Harold Scott.

PLAGUE.

LE GALL, R. La peste à Madagascar [Plague in Madagascar] Bull. Office Internat. d'Hyg. Publique. 1943 July-Aug v 35 Nos. 7-8 318-48, 2 charts & 1 map.

A detailed account with abundant figure data, is here given of 20 years of plague in Madagascar between 1921 and 1941. Plague appeared on the coast at various points as early as 1899 but always disappeared spontaneously until the disease obtained a footing on the central uplands at Tananarivo when it became endemic. A record of the index of contamination, or number of cases per 10 000 inhabitants shows 14.2 for 1921 and even higher figures year by year to 1932 with 30.4 and 1936 with 14.4 after which a marked decline took place exemplified in annual figures from 8.6 to 1.6. This diminution is directly claimed as due to the introduction of large scale vaccination with living E.V. plague bacilli. The septicaemic form, a bacteraemia, is in general terms only a terminal feature of either pneumonic or bubonic plague. Pneumonic plague is rather common in the high plateau region and is explainable as a respiratory disease of direct infection and due primarily to climatic conditions, in other words to the lowering of the temperature at least to below 15°C. (59°F) which is winter in the island. Plague as judged by mortality returns, has a high mortality of about 91.2 per cent. which however is a doubtful figure owing to the likelihood of concealment of cases by the natives as far as possible. This is borne out by the statement that some 95 per cent. of cases of plague are only diagnosed by organ smear post mortem.

The author has little doubt that the main vector of plague is the rat flea *Xenopsylla cheopis* and also stresses the fact that this flea can live in burrows in dark corners in rice debris, and in dust altogether away from its host the domestic rat. The rôle of man in the dissemination of plague appears to be secondary. A rat flea index too with the knowledge of possible existence of the flea apart from its host has become of much less interest to the epidemiologist. Continued examination of captured rats for plague infection seems to be superfluous and has been given up as a laboratory procedure. Out of 87 165 rodents examined between 1931 and 1935 only 0.12 per cent. were found to be carriers of plague bacilli.

It is natural that great emphasis should be placed in a review of plague in Madagascar on the prophylactic value of the E.V. vaccine of GIBARD and ROBIN [see this Bulletin 1943 v 40 777 1899 v 36 314]. Some striking figures are given of the reduction of incidence of plague after its introduction. Take the five years before it came into use 1930 to 1934 with incidence per 10 000 population respectively of 13.1 28.8 30.4 28.4 and 25.8 and compare them with those of five years when it was in use 1937 to 1941 with the figures 6.6 4.5 4.7 5.2 and 1.8. In fact the author roundly declares that the killed vaccine of the Pasteur Institute of Paris (previously used) was inefficacious. Treatment of plague has been on the lines of use of E.V. anti plague serum or

serum and sulphonamide especially sulphapyridine with excellent results in bubonic plague and no value in pneumonic plague. In conclusion the hope is expressed that plague like smallpox will soon have disappeared from the Great Island.

W F Harvey

WOODWARD Gladys E. The Ribonuclease Activity of *Pasteurella pestis* (Plague Bacillus) *J Biol Chem* 1944 Nov v 156 No 1 143-9 [13 refs]

What is shown by the data of this report is that living *Pasteurella pestis* cells killed by phenylmercuric nitrate and a cell free preparation decompose the ribonucleic acid of yeast and that the predominant action appears to be depolymerization. In the author's summary this is stated as follows —

Analytical data obtained from hydrochloric acid precipitation and uranium fractionation show that yeast nucleic acid is enzymatically decomposed by living cells of *Pasteurella pestis* cells killed by phenylmercuric nitrate and by a cell free preparation. Only part of the nucleic acid decomposed is hydrolyzed to mononucleotides the remainder probably existing in a depolymerized state

W F Harvey

HECHT O. Consideraciones entomológicas a la epidemiología de la peste bubónica de los roedores en Venezuela. [Entomological Notes on the Epidemiology of Bubonic Plague in Rodents in Venezuela.] *Rev Sanidad Asistencia Social* Caracas 1943 v 8 No 6 1159-62. [Summary taken from *Rev Applied Entom* Ser B 1944 Dec. v 32 Pt. 12, 231]

Details are given of the monthly collections of fleas from rodents trapped between March 1942 and June 1943 in the sylvatic zone of Aragua State Venezuela referred to in a previous paper. *Rhopalosiphum* formed 81.9-100 per cent. of the total in each of the 14 months for which records are given except May 1942. It then constituted only 27.5 per cent. *Xenopsylla cheopis* Roths and *X. brasiliensis* Baker forming 20.3 and 52.2 per cent respectively. The significance in relation to the transmission of plague of this occasional appearance of species of *Xenopsylla* in considerable numbers is discussed with special reference to the work of Eskey. A small epidemic of plague in man (19 cases) occurred not far away in July and August 1943. The percentage of *X. brasiliensis* had risen in June to 17.3 in the whole area and to 44.9 in the nearest sector but it was not possible to determine whether the two facts were related.

ANDERSON G F. The Flea Genus *Thersites* and Syriatic Plague with the Description of *T. bremani* n. sp. *J Parasitology* 1944 Aug v 30 No. 4 237-40 3 figs

BRAMBELL, F W R. & DAVIS D H S. The Normal Occurrence, Structure and Homology of Prostate Glands in Adult Female *Mastomys erythroleucus* Temm. Reprinted from *J Anatomy* 1940 Oct v 75 Pt. 1 64-74 6 text figs & 5 figs on 1 pl. [14 refs.]

— & —. Reproduction of the Multimammate Mouse (*Mastomys erythroleucus* Temm.,) of Sierra Leone. Reprinted from *Proc. Zool Soc of London* Ser B 1941 v 3 1-11 2 text figs. & 7 figs on 2 pls.

The multimammate mouse of S Africa (*Mastomys coucha*) is an important link between field and domestic rodents in the transmission of plague. *M. erythroleucus* may in the future be important in this matter and for those who may be called upon to study this rodent these two papers have their interest.

Charles Wilcocks

HUNDLEY J M & NAST H W Anti-Plague Measures in Tacoma, Washington.
Pub Health Rep Wash. 1944 Sept. 22, v 59 No. 33, 1239-53 4 figs.

Up to 1942 plague had not been declared in Tacoma. Its discovery in this year seems to have been something of an accident and due to the visit of a mobile unit of the United States Public Health Service "in the course of a routine check for the presence of plague infection. This unit trapped 257 rats near two large flour mills on the western waterfront of Tacoma harbor" and seven rats were found by isolation of the plague bacillus to be infected. The authors admit that it might be assumed that the plague had been present for many years and yet, no human case of plague by the records has ever occurred in Tacoma. What is most interesting in this record is that active measures were taken immediately as is obligatory under the Pan-American Sanitary Treaty "when plague is present in a seaport city. A full description of the measures taken is given—the preliminary survey and the control measures—such as trapping, poisoning, gassing, fumigation food sanitation, harbourage elimination rat proofing, quarantine and educational activities. These measures were crowned with success and at the very low cost of 56,742 dollars for the year. Compare this expenditure in which trappers were paid the high figure of 200 dollars a month, with that of San Francisco for 11 months 561 143 dollars, Oakland of 65 000 dollars, and Seattle 65 000 dollars. Moreover about 5 000 dollars of the expenditure remains in capital equipment for a future permanent programme.

"On May 4 1943 the last positive specimen was found. Since then more than 8 000 rodents and their ectoparasites have been examined without detecting the presence of plague. It therefore seems reasonable to conclude that the infection has been brought under complete control and that plague has been eradicated in Tacoma. W F Harvey

CHOLERA.

ROGERS, L. Cholera Incidence in India in relation to Rainfall, Absolute Humidity and Pilgrimages. Inoculation of Pilgrims as a Preventive Measure. *Trans Roy Soc Trop Med. & Hyg.* 1944 Nov., v 38, No 2, 73-89 Discussion 89-94 (GILL, C. L. JAMES S. P. COLLINGWOOD F. C. ROGERS L. (in reply))

Two distinct parts constitute this paper. It follows the lines already made familiar by the extensive researches of Sir Leonard Rogers which have resulted in the formulation of positive factors in the spread of cholera in India. As the timing of pilgrimages is known and rainfall and absolute humidity are measurable they have undoubtedly provided a most important method of forecast of the outbreak of cholera on an epidemic scale. All sanitary authorities in India will use this helpful approach to the problem. Rogers brings, with proper emphasis, new and additional data to uphold his contentions and statistical students of epidemiology as well as practical sanitarians, will study his tables and explanations very carefully to determine the concordance of calculated and observed figures. The sanitarian in India will take note of the condensed conclusion. "A close watch on the June to October south-west monsoon rains enables high cholera incidence to be foreseen in the autumn months in the endemic areas with absolute humidities always over 0-400 and several months before the spread of epidemics of cholera in the next spring from the endemic to the epidemic areas. The danger of cholera being spread by the return of

pilgrims from any particular Fair can also be foreseen from the climatic data at the time and a knowledge that cholera is present in the areas through which the pilgrims have to travel.

A somewhat lively and very interesting discussion took place after the reading of the paper which was concentrated for the most part on the practical expediency and the efficacy of cholera inoculation as a preventive of devastating outbreaks. Colonel GILL touched lightly on the bionomics of the cholera vibrio in his reference to transmission of cholera through the agency of importation by sacred water or sweetmeats. In respect of cholera vaccine however he bluntly says of the vaccine of his own time that cholera inoculation gave no sort of solid immunity. The people of the Punjab do not like compulsion and the large scale compulsory plague inoculation in the Punjab of earlier days came to a sudden unfortunate end with riots and bloodshed. That large-scale trial would have afforded some very useful data if it had been completed. Colonel JAMES with his own personal experience of cholera inoculation which was also that of Colonel Gill continued the adverse commentary beginning with the remark that the material with which Haffkine made the first anti-cholera inoculations in Bengal in 1896 was probably less effective than the vaccine now available. [This is interesting in view of the stress which is now being laid upon the use of living instead of dead vaccines in prophylaxis of other diseases. Some of Haffkine's earliest vaccines were composed of living organisms.] A very important addition to the discussion contributed by James is embodied in the remark Cholera is the best example of a tropical epidemic disease which is amenable to improvements in environmental domestic and personal sanitation. Everyone agrees that India is greatly in need of improvement in those respects as well as in getting more and better food more and better education and a higher standard of living generally. [It is surprising that the discussion did not elicit any remarks on the possibility of cure being better than prevention that is to say of the possibility that curative drugs may be discovered which may prove better than a prophylactic inoculation on any compulsory large and expensive scale.]

W F Harvey

FEISENFELD O The Lecithinase Activity of *Vibrio Comma* and the *El Tor* *Vibrio* *J Bacteriology* 1944 Aug v 48 No 2 155-7 [13 refs]

Sensitive tests are now applied in the examination of lecithinases. Three types A B and C have been named. In the present study four *V cholerae* strains and one *V El Tor* were available and the lecithinase activity of all these vibrios showed the effects of lecithinase B choline-phosphatase and glycerophosphatase resulting in the production of free phosphate choline and fatty acids. The optimal temperature for this activity was 36-38°C and the optimal pH 7.4 to 7.6. Stimulants of the reaction were found in Ca and Mg, but sulphonamides and barbiturates were without effect. Formaldehyde phenol and fat-soluble narcotics exercised an inhibitory action. Whether this effect of formaldehyde helps to explain the mechanism of the detoxication of culture filtrates (toxins) through formol remains to be investigated.

W F Harvey

INDIAN MED GAZ 1944 Oct v 79 No 10 477-9 5 figs. Intravenous Transfusions in Cholera and other Conditions A Note on Technique

In cholera cases where collapse and dehydration figure prominently it may be quite a difficult matter to get the transfusion nozzle into a vein in the usual way. The method here described is one of operation to expose the vein is very simple and is fully illustrated. It has long been used in the cholera wards of the Campbell Hospital Calcutta. After exposure of the vein two ligatures are

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applied above and below the position of entry. The lower ligature only is tied. The vein is then transfixed from side to side with a surgical needle curved on the flat, so as to pass clean through the lumen. An incision is made through the vein on the needle, also from side to side and the needle withdrawn. The eye of the needle is used to lever up one lip of the opening to facilitate the insertion of the transfusion nozzle and the upper ligature is tied tightly over the nozzle. It seems probable that this rapid, simple and effective method might be of use in other conditions where entry into a vein is difficult. W F Harvey

GRIFFITHS J J Mouse Protective Antibodies in Human Serums following Injections with Cholera Vaccine. *Pub Health Rep* Wash. 1944 Oct. 20 v 59 No. 42, 1374-84 1 fig

In war time large numbers of men become exposed to the risk of infective diseases who would not ordinarily have to face any such risk throughout life. One of the regular methods employed to counter the risk both in the last war and in this, has been prophylactic inoculation of vaccines. A quantitative assessment of the value of this vaccination is very desirable and—apart from statistical results—is usually measured in terms of antibody response. Most convenient is the measurement of agglutinin titre which was done in this case on 34 white male medical student volunteers of 21 to 36 years of age, vaccinated with Inaba and Ogawa strains in equal amounts. One objection to the use of the agglutinin titre is that it may not be a sufficiently true measure of immunity. The author has departed from this stereotyped measure by carrying through intraperitoneally and, one hour later of varying doses of living vibrios in mucin also intraperitoneally according to the methods of SILER and others of the United States Army Medical School. Results may be summarized as follows — "Mouse protective substances appeared in the serum of human volunteers 1 week following vaccination. These antibodies were present at least 18 months after vaccination and were more concentrated in serums at 1 week and 1 month than at 3 or 6 months. In this study no definite correlation between height of agglutinin and mouse protective titers could be made. W F Harvey

BACILLARY DYSENTERY

FINKMAN W B & WEISS J E Control of Bacillary Dysentery in a Tropical Outpost. Report of 1,000 Cases. *Bull US Army Med. Dept.* 1944 Oct. No 61 71-82.

The point of particular interest in this report on bacillary dysentery concerns the effect of increasing the dosage of sulphaguanidine. The predominant isolated on S.S. or desoxycholate-citrate agar was *Bact. flexneri* and cases were classified as mild moderate or severe "dysentery" or "enteritis" according as a specific dysentery organism was or was not isolated on admission. In the first series of cases, the daily dosage of sulphaguanidine was 6-7 gm continued for average periods of seven days in mild and moderate dysentery infections, 12 days in severe infections, 6 to 9 days in acute enteritis and 7.5 and 6.5 days in contact and convalescent carriers. The drug was discontinued when one negative stool culture had been obtained, the patient was discharged after three further consecutive negative examinations. In this series, there were 34 carriers and two clinical relapses among

280 treated cases of dysentery 13 carriers and four relapses among 200 treated cases of acute enteritis 25 carriers and four relapses among 120 cases of enteritis treated symptomatically, and eight persistent carriers among 245 treated contact and convalescent carriers. There were no drug reactions.

In the second group 3.5 gm. of sulphaguanidine was given to all acute cases on admission followed by 12 gm. daily until stools were fewer than five per day and then 9 gm. daily. Drug was continued for average periods of 15 to 17 days in the dysentery cases, for 14 to 19 days in the enteritis cases and for 8-7 days in doses of 9 gm. daily in the contact carriers. Treatment was discontinued after three consecutive negative stool cultures and the patient was discharged after three more successive negative examinations. The higher dosage and the longer period of treatment resulted in no carriers or relapses among 69 cases of dysentery no carrier and one relapse among 80 cases of enteritis and two persistent carriers among 91 contact carriers. There were two instances of drug reaction in this group one a drug rash with fever after eight days therapy the other drug fever after six days therapy. The authors stress the importance of the dysentery carrier and state that 'frequent stool examination of food handlers follow up stool studies of discharged hospital cases and the examination of all troops arriving at and leaving this command were excellent concomitants of good sanitation in preventing bacillary dysentery. In the control of the carrier state these methods reduced the rate from 11 per cent. to less than 0.3 per cent.

Robert Cruickshank

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

OSBURN H. S. Amoebiasis in Infancy. *Clin. Proc.* Cape Town. 1944 Oct v 3 No 8 405-12 3 figs. [10 refs.]

Amoebiasis is by no means unknown in infancy. HOWELL and KNOLL [this *Bulletin* 1941 v 38 267] found 18 cases in 11 years in ages ranging from 8 months to 13 years.

BECKER [this *Bulletin* 1937 v 34 950] in analysis of post mortem material at Johannesburg found amoebic infection more or less evenly spaced throughout the age-groups in the Bantu whilst in the Europeans no cases were discovered among 64 autopsies in the first 20 years of life. Becker however admits that his numbers are probably too small for conclusions to be significant. In 21 native patients in the Salisbury and Charter districts of S. Rhodesia with active *E. histolytica* in the faeces Osburn found that three were under five years and one of these was under two years of age. An autopsy on another female child under two years revealed amoebic ulceration of the large intestine and numerous amoebic abscesses of the liver. This contained four large abscesses in the right lobe varying in size from that of a golf ball to a tangerine orange and in addition there were very numerous miliary lesions [the figure shows also a fifth large abscess]. Each of the larger lesions was surrounded by a broad haemorrhagic zone in places half an inch wide. Three were adherent to the parietal peritoneum and were ruptured in removing the liver. The most anterior in the right lobe was adherent to the transverse colon. The walls were shaggy and necrotic. Typical amoebic ulcers were present in the large intestine tending to coalesce in the caecum but discrete in ascending and transverse colons. In the upper colon the faeces were dark yellow but not dysenteric in character.

Although the autopsy was performed after a lapse of 20 hours the pus taken from a scraping just within the yellow necrotic margin of an abscess revealed

amoebae which contained red cells and were still motile [illustrated by serial drawings to demonstrate protrusion of pseudopodia]. Numerous forms of *E. histolytica* were present in the walls of the abscesses on section as well as in the caecum and terminal ileum, together with well-marked lymphocytic infiltration and moderate numbers of endothelial cells.

The author emphasizes the rarity of hepatic amoebiasis in the female, for out of 28 other cases collected by him in Zulua and Rhodesian natives, all were in males. The large number of abscesses present was also remarkable.

It is suggested that further investigation might reveal that this occurrence is not quite so exceptional as might at first sight appear for in the Enkeldoorn Hospital between September 1942 and May 1944 there were admitted five cases of amoebiasis in children to eleven cases in adults—a ratio suggesting a distribution of infection very different from that usually reported.

P. Manson-Bahr

PARRY E. Intussusception complicating Amoebic Dysentery *Lancet*. 1945 Jan. 13 50.

PAL, J. C. MUKERJI B. GUPTA, J. C. & CHATTERJEE M. L. The Quality of Indian-Made Synthetic Drugs. II Examination of Iodochlorhydroxyquinolins (Enterovioform) of Indian Manufacture. *Indian Med. Gaz.* 1944 Oct. v 79 No 10 469-71

"Indian-made iodochlorhydroxyquinoline differs slightly in ash content from the standard product of the same name in N N R 1941 but agrees closely in melting-point physical characteristics solubility iodine and chlorine percentages with the Ciba brand Enterovioform. Its toxicity (one brand only tested) is within safe limits in therapeutic dosages. In clinical trials in controlled cases of amoebiasis in hospitalized patients, it has given comparable satisfactory results.

"The Indian-made synthetic product is therefore likely to be of the proper standard and wider clinical trial to these brands can be given by the Indian medical profession in suitable cases without any risk to their patients when employed in therapeutic doses.

SMITH LU CHANG Destruction of Micro-Organisms. *J. Amer. Water Works Ass.* 1944 Nov v 36 No. 11 1192-207 17 figs on 1 pl. [23 refs]

The author has shown previously [CHANG and FAIR this Bulletin 1942 v 30 313] that by using a solution of ortho-toluidine [for concentrations of chlorine below 2 p.p.m.] penetration of chlorine into cysts of *E. histolytica* could be demonstrated when the cyst had been exposed to large doses of chlorine as gaseous chlorine and H.T.H. (high test hypochlorite) or chloramines at pH 5.0. This penetration of chlorine increased with increase in the chlorine dosages and the contact periods as judged by the greater intensity of the yellow coloration of the cysts. It was also shown that the cyst-penetrating power of chloramines was much weaker than that of gaseous chlorine and H.T.H. Furthermore, associated with this penetration changes of destructive character were observed in the nuclei within the cysts and it seemed probable that the death of cysts, following exposure to chlorine, was the result of these cytological changes. In the study reported in the present paper more extensive tests were made in an attempt to answer a number of questions—(a) Do different chlorine and chloramine compounds differ in their penetrating power? (b) Is there a parallel between the cysticidal power and the penetrating power? (c) How do the pH and the contact period affect the penetrating power?

(d) Does the supposed nascent oxygen liberated by HOCl play any significant part in the destructive process? (e) Is destruction or poisoning the actual cause of death?

Tests were carried out by adding five drops of a cyst suspension (containing 10 000 to 50 000 cysts) to 40 cc. of various solutions of chlorine and chloramine compounds (at desired concentrations of chlorine and pH values) which had been allowed to stand for four hours till Cl_2 , HOCl, OCl^- , NHCl_2 and NH_2Cl and hydrolysis products of organic chloramine compounds if any had reached equilibrium. After the desired contact period the sediment in each tube was washed by centrifugation with distilled water taken up in 5 cc. distilled water to which a few drops of ortho-toluidine solution was added. Excess of the yellow liquid was washed away by distilled water and the centrifuged deposit submitted to microscopic examination for degrees of yellow coloration of the cysts. The viability of cysts after exposure to the cysticidal agents was tested by washing them and inoculating them to liver infusion agar medium while cytological changes were studied by making films on slides smeared with egg albumin fixing on Schaudinn's fluid and staining with iron haematoxylin.

As a result of these investigations it was found that when cysts were exposed to solutions of gaseous chlorine, LTH, dichloramine, monochloramine, Halazone and succinchlorimide penetration of chlorine occurred. The penetrating power was in the order Cl_2 , HOCl, Halazone, dichloramine, succinchlorimide and monochloramine. The greater the concentration of titratable chlorine and the longer the contact period the greater was the penetration. The effect of pH on the penetrating power of gaseous chlorine was due to the formation of Cl_2 , HOCl and OCl^- the quantities of which increased in this order as the pH rose from 2.0 to 8.5. The pH effect on chloramines was due to the formation of di- and mono-chloramine. In the case of Halazone it seemed to be due to the hydrolysis product HOCl. The effect on succinchlorimide was not significant. The good penetrating power of Halazone and dichloramine was attributed to the hydrolysis product HOCl. Succinchlorimide and monochloramine were not hydrolysed. The penetrating power of these agents was parallel to their cysticidal efficiency. Hypochlorite (OCl^-) was found to be non-penetrating and non-cysticidal. It was thought that the action of chlorine and chloramine compounds was attributable to the active chlorine oxidizing or chlorinating the proteins. It was unlikely that nascent oxygen liberated by HOCl played any part in the process. Definite destructive changes in the cysts illustrated in a series of microphotographs occur after exposure to minimal doses of chlorine. It would seem that these changes render the cyst non-viable before oxidation of the proteins or chlorination of these to form chloramine which would poison the cysts can take place. C. M. Wenyon

WELCH P. B. Giardiasis with Unusual Findings. *Gastroenterology* 1944 Aug. v 3 No 2 88-102.

In a previous paper (*Amer. J. Digest. Dis.* 1943 v 10 52) the author reported upon 13 cases of giardiasis in which radiological evidence was obtained of functional or anatomical changes in the duodenum, duodenal cap, pylorus and prepyloric area of the stomach. Examination of the blood in 12 of the cases revealed an eosinophilia in 58 per cent. After atabrine (mepacrine) therapy six of the cases showing eosinophilia were re-examined and in five the condition no longer existed. In the present paper an account is given of 16 further cases, eight in adults and eight in children—giving a total of 29 cases in the two series. Radiological evidence of functional or anatomical changes was found in three-fourths of all the cases and leads to the suggestion that alterations in the peptic area are characteristic of severe giardia infection. Furthermore

in 22 of the 29 cases there was an eosinophilia varying from 4 to 13 per cent. In 18 of 21 of these eosinophilic cases there was a return to normal after atabrine therapy. In 15 cases there was a leucocytosis (10 000 or over). In all of these a drop occurred after atabrine treatment. C. M. Wexley

RELAPSING FEVER AND OTHER SPIROCHAETOSIS

BULMER, E. Weil's Disease in Normandy. Its Treatment with Penicillin. *Brit Med J* 1945 Jan 27 113-14

During the present campaign in North-West Europe sporadic cases of Weil's disease have so far (Dec. 1944) been met with only in Normandy. They all occurred from the middle of July to the end of September during which period the author had been informed of 39 cases. However since all except two of these patients showed well developed jaundice, it is probable that many cases were missed and the author estimates that about 100 cases may have occurred.

Spirochaetes were found in the blood in several instances and often in the urine. In most cases positive agglutination tests were obtained by sending the blood to the U.K. Sixteen of the patients were treated with penicillin, 40 000 units three-hourly the average total amount given being about 1 125 000 units. The treatment seemed to shorten the duration of the fever and to reduce the number of relapses. Also there was a very general clinical impression that the treated patients improved dramatically within 36 hours. On the other hand, penicillin did not seem to influence the degree and duration of cholaemia, nor to affect the rate of disappearance of icterus from the skin or of bile from the urine. It also did not affect the degree of nitrogen retention or the rate of disappearance of albuminuria.

One out of the 16 treated patients died of uraemia. Two out of 23 untreated patients died, one of myocarditis and the other of uraemia.

The author considers that further work on the treatment of Weil's disease with penicillin is desirable. It seems essential to give the treatment early and the dosage should be high. E. Hindle

CARRAGHER, A. E. A Case of Weil's Disease treated with Penicillin. [Memoranda.] *Brit Med J* 1945 Jan 27 119

The history of a soldier invalided from France with pyrexia of six days duration who reached a hospital in Wales on September 12th 1944. He stated that during August he had bathed frequently in a rat infested river in Normandy. Spirochaetes were found both in the blood and urine and the patient's serum agglutinated *L. icterohaemorrhagiae* to a titre of 1:1600.

Penicillin therapy was started with 20 000 units intramuscularly three-hourly for four days and then four-hourly for another three days the total dosage being 900 000 units. The condition of the patient improved markedly within a few hours and spirochaetes disappeared from the blood and urine within 15 hours of the first injection. The patient did not develop an after fever and was discharged perfectly well within 17 days. E. Hindle

AUGUSTINE D. L. WEINMAN D. & McALLISTER, JOHN. Penicillin Sodium Therapy in Experimental Weil's Disease. *New England J of Med* 1944 Sept. 7 v 291 No. 10 353-9

The authors used a strain of *Leptospira icterohaemorrhagiae* which was very virulent for guinea-pigs killing them within seven days. Two experiments

were made. In the first experiment 10 guineapigs each 180 gm in weight were inoculated with the spirochaetes and showed jaundice on the fourth day five were then injected intraperitoneally with 4 000 Oxford units of penicillin sodium in 1 cc. of saline every four hours for 78 hours or until death occurred while the other five were kept as controls. Of the treated guineapigs one died after 4 000 units two after 8 000 and the remaining two died on the morning after the final injection (total 48 000 units). The controls died before the last two of the treated animals did. At autopsy all the animals showed similar characteristic lesions with motile leptospirae in the liver and kidneys.

In the second experiment eight guineapigs were similarly infected but the treatment of four was begun 38 hours after inoculation and each was given 5 000 units of penicillin sodium intraperitoneally every four hours for 48 hours (total 60 000 units). Of the controls, one died on the third day and two on the seventh day and showed lesions of Weil's disease at autopsy. The fourth guineapig recovered and was killed on the 15th day after inoculation the organs being apparently normal. None of the treated guineapigs showed jaundice or other signs of illness except roughness of fur. One was found dead on the fourth day after completion of treatment, another on the fifth day and a third on the seventh day. At autopsy leptospirae were found in the liver and kidneys but there were no severe lesions. The last guineapig was killed while in apparently good health on the 11th day after treatment (15th after inoculation) the organs appeared to be normal and no spirochaetes were seen.

Penicillin therefore seemed to have some suppressive effect but was not curative. The results differ from those of HEILMAN and HERRELL (this *Bulletin* 1944 v 41 758) they however used a strain of leptospira of low virulence and gave penicillin 12-24 hours after inoculation. J. F. Corson

AFRIQUE OCCIDENTALE FRANÇAISE. RAPPORT SUR LE FONCTIONNEMENT TECHNIQUE DE L'INSTITUT PASTEUR EN 1942 [DURIEUX C.] pp 81-4. Étude d'un spirochétidé isolé du sang de l'homme au cours d'une maladie fébrile. [The Study of a Spirochaete Isolated from Human Blood during a Febrile Attack.]

An African child showed a temperature of 39.5 to 40°C which lasted for 15 days accompanied by slight clinical symptoms including enlarged liver and headache after which the patient recovered. There were no signs of jaundice. Leptospiral organisms were isolated from blood collected on the fifth day of the disease by means of culture in ordinary broth. Attempts to infect guinea pigs rabbits rats and mice were negative but two inoculated monkeys *Cercopithecus palas* showed signs of infection. One died after 22 days and although the autopsy was negative leptospirae were recovered by blood culture. The second monkey showed vague symptoms including loss of appetite and was accidentally killed after 28 days. Leptospirae were also recovered by culture of heart blood.

It is considered that this may be another leptospiral infection related to mud fever. E. Hinde

YAWS

FINDLAY G. M. HILL A. R. & MACPHERSON A. Penicillin in Yaws and Tropical Ulcer [Correspondence.] *Nature* 1944 Dec 23 785-6

Penicillin was found to be effective in a trial in the Gold Coast in 24 cases of yaws in children and 25 cases of tropical ulcer.

Yaws.—Two cases were primary 22 secondary the patients were given 50 000–100 000 Oxford Units of penicillin intramuscularly during 12–24 hours.

The results were dramatic and nineteen cases were clinically cured in an average time of 6½ days. The two cases of primary yaws were cured completely with reversal of the result in the Kahn test within seven days. In the cases of secondary yaws the "snuffles" disappeared the papules desquamated, and the yaws dried up within 24 hours and in 2–10 days only scars remained. In a case with severe bismuth stomatitis, penicillin cured both the yaws and the stomatitis within 48 hours. There have been no toxic results. In two cases of secondary yaws observed for six weeks the result of the Kahn test was not reversed but the authors think that larger doses—500 000–1,000,000—would produce reversal.

Tropical ulcer.—Many of the ulcers were several months old. They were treated by the injection of 100 000 Oxford Units in 24 hours and the application of penicillin ointment (250 units per gm.) In some cases the local application only was used. Great improvement took place within 24 hours granulations filled the base of the ulcer and epithelialization began at the edge. Within a few days the ulcers became practically sterile.

Carcum oris.—Two severe cases in children were greatly improved and one recovered. J. F. Corson.

LEPROSY

BRITISH EMPIRE LEPROSY RELIEF ASSOCIATION (MADRAS PROVINCIAL COUNCIL) Annual Report 1943–44 (Austin T. Chairman Executive Committee) 20 pp. 1944 Madras Diocesan Press.

This report appears to have been written by the Hon. Secretary Dr R. G. COCHRANE, and deals in part with the same matter as in the following paper by him. The main facts recorded will be dealt with under this heading and the general considerations under the following paper.

An advance is reported in an order for the admission of cases of leprosy to general hospitals and in arrangements for the instruction of the students of Madras Medical Colleges by an expert on leprosy. Epidemiological enquiries have been continued through village surveys regarding which statistics are recorded to show a gross incidence of 21.7 per mille and a child rate of 28.8 per mille—very high rates. The open case rate was only 11.5 per mille in an area with poor economic conditions. Repeated surveys confirm the earlier conclusion that abortive lesions have a great significance. In the development of lepromatous cases, incipient lesions of childhood in the form of simple macules, including neural macules, play an important part and may be classed as pre-lepromatous in nature. The night segregation of infective cases in villages, to lessen their contact with susceptible children, has been followed by a reduction in child infections. It is proposed to examine all school children in Madras City for signs of early disease and to allow contacts to be traced, but a leprosy hospital to hold 500 infective cases is urgently needed. Uninfective crippled beggars could be provided for by a religious body. It is estimated that in Madras city there are 5,000 to 7,000 cases of these—at least 500 to 750 are probably infective. A children's Leprosy Sanatorium at Ettapur admitted

31 boys during 1942 discharged 17 and had 39 remaining at the end of the year. Such institutions should be multiplied. Surveys show very great variations in incidence (from nil to 124 per mille) in villages close to each other. There is much greater contact with infective patients in some villages than in others. In an anti leprosy campaign highly infected villages should be sought out and dealt with. As elsewhere lepromatous cases gave negative lepromin reactions. Work on the Wassermann reaction showed increasing positive results with the advance of lepromatous cases without any indications or history of infection with syphilis. These were consequently the direct result of leprosy infection.

L. Rogers

COCHRANE R. G. *Leprosy Control with particular reference to the Madras Presidency* *Indian Med Gaz* 1944 Sept v 79 No 9 438-45

The author discusses the present position and needs of leprosy control in India in the light of his last eight years' investigations in Madras. He first endorses the recommendation of the Manila Leprosy Conference of 1931 to drop the word leper from the medical vocabulary. He believes that with adequate finance and personnel the disease can be controlled, but that patient treatment alone is not sufficient, though even in lepromatous cases early and intensive treatment gives a good chance of recovery. He discusses anti leprosy work under a number of headings. Leprosy institutions are required in all districts in which surveys reveal serious prevalence of the disease to provide both segregation and treatment of open (that is infective) cases. In addition to the large Lady Willingdon Leprosarium at Chingleput five smaller institutions under the Mission to Lepers require to be modernized and enlarged, each to accommodate 400 cases under two doctors with agricultural and industrial occupation. Courses of instruction on leprosy to medical practitioners should be longer than fourteen days as at present. Surveys on the lines long ago introduced by MUTR (*Leprosy in India* 1931 v 3 50) are essential to enable the seriously infected areas to be located and dealt with. Rural units should be established where required together with village or family segregation. Among the 90 per cent. of the population engaged in the day time in agriculture night segregation of infected cases may do much to lessen the danger to children. For urban conditions he advocates either isolation in an institution or home isolation with a separate room, bedding, cooking utensils, etc. but admits the difficulties in enforcing such regulations and that this is only possible in the case of those with sufficient means. All municipalities should therefore provide an institution for infective cases. In no other way can the problem be solved and the sooner this is realized and provided for the quicker will leprosy be controlled. Special sanatoria for children are also advised because they cannot be isolated at home. The child contacts of infective cases should be examined periodically for early symptoms. Deformed and derelict cases and beggars should be provided for by philanthropic institutions. Propaganda must be continued to educate public opinion. The Madras Public Health Act is being modified to bring it up to date and to compel the infective patients to isolate themselves or to submit to compulsory segregation. At present no distinction is made between open and closed cases. Facilities for segregation will have to be provided, but compulsory measures should be used only in cases of emergency. No success can be expected unless a well qualified medical officer is placed in charge of the campaign in each province.

L. Rogers

LEPROSY IN INDIA 1944 July v 16 No 3 109-13 The Annual Report for 1943 of the Indian Council of B.E.L.B.A.

PRETORIA LEPROSY INSTITUTION Minutes and Papers of a Conference on Leprosy held at Pretoria Leper Institution on 18th & 19th September 1944. 51 typed pp. & 1 folding chart.

This important South African leprosy conference was attended by the members of the Leprosy Board and medical officers from the institutions of South Africa, Basutoland and Southern Rhodesia, and the papers dealt with below were read. The following are the more important recommendations — The occurrence of relapses in probationally discharged cases should be further investigated, together with the tests made before the discharge of patients. Better control of those discharged should be carried out by periodical examinations by a leprologist. District surgeons should be induced to revise their knowledge of leprosy by further courses of instruction to enable them to recognize the signs of recrudescence of the disease. The question of Native inspectors should be investigated. University instruction on leprosy should be given with the aid of coloured films and photographs. Demonstrations of methods of treatment, etc. were also given by members present. The question of home segregation was discussed and objections were raised to this being allowed in cases positive bacteriologically on the ground that it was impossible to ensure that the regulations were always faithfully carried out. Brief discussion took place on some of the following papers which were read at the meetings.

Some of the Problems of Leprosy was the title of a paper by Dr F S DREWZ of the Mambati Leper Institution, where he had worked for 25 years. He points out that we have no certain knowledge regarding the mode of entry of the *M. leprae* into the human system, and suggests the tonsils as a possible site, although he has never found the organism in smears from them. He next discusses types of leprosy in relation to the resisting powers of the infected, quoting from various writers. He suggests that the early lesion consists of a small-cell infiltration which might later progress to either tuberculoid or lepromatous changes. Drewz mentions the observation of Dr Fox of the South African Institute for Medical Research that the diet of natives of the Transkei is seriously deficient in calcium, and thinks that this might influence their resisting powers. He states that in some cases all lepromatous nodules disappear during the two or three days before death from tuberculosis. He advocates a period of complete rest, good food and fresh air for leprosy patients on the lines of sanatorium treatment of pulmonary tuberculosis in order to increase their resistance. Good results are obtained from injections of up to 14 cc. of ethyl esters by infiltration at the base of the nodule rather than by injections of small doses into them. Neural macules respond to intradermal injections. He has not found the sedimentation test of much prognostic value but the lepromin test is more reliable.

Criteria of Cure by A. R. DAVISON Pretoria Leper Institution.

The occurrence of reactions in 12 of 15 probationally discharged patients who had been detained on humanitarian grounds raised the question of the standard of cure or arrest, which has never been definitely laid down. The present custom is to require 12 negative smears at monthly intervals except in the case of a new admission in an obviously burnt-out stage. Further the patient must show no raised or red macules and no new ones. A case is considered to be clinically reactive if after a period of quiescence new lesions break out or old ones become raised or red. A survey of probationally discharged cases is being arranged but only nine local cases have yet been examined one of which was reactive. Hitherto all discharged patients are examined by a district surgeon every six months for the first three years and every 12 months for three years more. Davison found 12 of 38 discharged cases in one district to be recrudescant but all of them were ill housed, ill-clothed and ill fed. He therefore advises that

before discharge patients with nerve leprosy should be free from all activity for 12 months and that in those previously bacteriologically positive 24 monthly smears should be negative including at least eight skin smears and X-rays should show no dead bone. Further the examinations by the district surgeons should be made every three months and the patients discharge chart should be sent to them instead of being pigeonholed by the magistrate, as at present the district surgeons should have a good knowledge of leprosy. Each case however should be examined by a leprologist once a year.

Leprosy Institutions by A. R. DAVISON

The author deals with the planning of a leper institution in a country with the fairly low incidence of 1 to 2 per mille and with no stinting of the money necessary to bring the policy to a successful conclusion [South Africa and the Southern U.S.A. are probably about the only leprosy infected countries which fulfil those conditions.] He considers that the sparseness of the population and the conflict with the South African policy of segregation make out patient treatment centres unsuitable. He also objects to leper villages on account of the infertility of the soil which would necessitate immense tracts of country being set aside if the patients are to subsist on its produce. This leaves only leper settlements with attached hospitals preferably to deal with a minimum of 1 000 patients so as to allow of two or more doctors being employed one of whom should be a research worker. The lay staff should include a gardener farm manager. The site should be within 10 miles of a town, and smallholdings should be allotted to patients and their produce bought by the institution. Segregation of the sexes is essential. The superintendent should have magisterial powers but native courts should try most offences. Committees of the patients should be formed and general meetings held each year to discuss policy and procedure. The families of breadwinning patients should receive maintenance grants.

Compulsory Segregation by A. R. DAVISON

The author begins with quotations from medical literature in support of his belief that although under normal conditions leprosy has a low degree of infectivity yet under conditions of poverty and malnutrition as in Nauru Islands the degree can assume almost epidemic proportions. He goes on to say that the only argument against segregation is its expense. On the importance of segregation he quotes from the Leprosy Commission of the League of Nations which states that 'it may be administratively possible and advisable to make it compulsory' and from the Cairo Congress on the methods of isolation of open cases in institutions villages or in the patients homes the last is the least effective. He considers that the conditions in South Africa are by no means unfavourable for the spread of leprosy and holds that the conditions would be worse today if there were no segregation. Since 1916 the European cases have declined from 188 to 74 the Cape Coloured cases numbered 345 in 1913 and are 120 today. The decline among the natives is less but it is certain that cases among them are now being seen in an earlier stage. The average duration of the disease prior to admission used to be about nine years today it is nearer two years. He agrees that in countries with large numbers of leprosy cases compulsory isolation in institutions is out of the question because the expense would be out of all proportion to the financial resources. South Africa is one of very few countries that can afford to carry out a policy of compulsory isolation for all stages and types of the disease and he concludes that by its means the disease is being controlled if not stamped out and that any relaxations of that policy could lead to an alarming increase of the disease. [Not long ago the cost of compulsory isolation in South Africa was a little over £50 per head.]

Conjugal Infections in Leprosy is the subject of a short note by B. MOISER of Southern Rhodesia. The rate of conjugal infection in 700 of his cases is only 1.57 per cent (a much lower figure than that given by ROGERS in *Leprosy*). In his institution he advises that married couples should not be separated when only one is infected. He suggests that the low rate of infection in such couples may be related to sex hormones which should be investigated in the hope of being able to make use of sex hormones prepared from leprosy patients in treatment.

In his paper *The Transmission of Leprosy* MOISER reports that 69 per cent. of cockroaches at Ngomahuru caught in the hospital grounds or in kraals in the Native Reserve, show in their gut or faeces acid fast oval bodies which, he thinks, are worthy of investigation in view of the number of leprosy infections he has seen in which family or other contact could not be traced.

The Campaign against Leprosy in Transkei by P. A. THORNTON

This paper deals with leprosy work at the Emjanyana Leprosy Institution South Africa and the author attempts to estimate the value of the leprosy Campaign carried out during the last ten years in Transkei which has an estimated population of a million and a half. The author opens with a statement that in the previous month 569 patients with active leprosy were seen by the medical board and that 148 had been recommended for discharge. During the previous five years there had been an average annual admission of 37 fewer cases than in the previous five years but the decrease may be due to the fact that there are now fewer practitioners doubtless because of war demands. During the last ten years 27.3 per cent. of all patients had been discharged all were neural cases which form just over half the numbers in the institution. There has been some increase in recrudescences but not an alarming one with readmissions after an average of about three years but very few were positive for bacteria and many of them came for surgical treatment. The methods of surveillance of discharged patients needs revision. He concludes that the campaign is apparently meeting with a small degree of success and that methods of treatment at present used are fairly successful.

Emjanyana Leprosy Institution.

Period 1935 to 1944

	1935	1936	1937	1938	1939	1940	1941	1942	1943	1944
Admitted for first time	180	217	207	254	174	210	181	172	151	145
Numbers seen by Board	598	601	649	683	654	670	608	600	543	569
Discharged as Arrested	114	146	193	206	203	144	249	138	181	146
Percentage of Discharges ..	12.5	24.3	30.1	31.6	30.7	21.5	40.9	23	33.3	25.6
Recrudescenced Cases	18	8	4	13	12	31	26	23	30	35
Death	70	79	54	67	64	43	59	69	55	71

L. Rogers

AUSTIN C. J. Central Leprosy Hospital, Makogai (Annual Report for 1943)
Fiji Legislative Council Council Paper No 17 1944 7-9

In 1943 the number of patients at the beginning of the year was 645 the admissions numbered 77 the discharges 65 28 died and 631 remained at the end of the year a reduction of 14. Of a total of 942 patients admitted in ten

years 295 came from Pacific Islands beyond the Colony of Fiji in the same period 75 were readmitted 17 of whom were again discharged. Of the 77 admitted during 1943 17 were Fijians 20 Indians 32 Cook Islanders 5 Samoans 2 Niue Islanders and 1 Euronesian. Of the 32 Cook Islanders no less than 24 were early Neural 1 cases so it is not surprising that a high proportion of those discharged were persons from those islands. Of 64 conditionally discharged 52 were Neural 1 and Neural 2 four were Lepromatous-1 and eight Lepromatous-2 cases and one formerly discharged lepromatous case was readmitted with retrogression. Among the Cook Island cases there were far more who were relatives of other lepers than among other communities and many of them were children so without care the disease would soon assume a far more threatening aspect. An important feature of this institution is the amount of paid work the inmates do both in agriculture and handicrafts for their earnings amounted to £2,890 in the year. A Fiji branch of the Lepers Trust Board has also been formed to assist those in need. Progress is thus being made in many ways in this up-to-date institution under the care of Dr Austin.

DEGOTTE J Contagiosité de la lèpre neurale Enquête épidémiologique chez les Pygmées [Infectivity of Neural Leprosy Epidemiological Study among the Pygmies] *Rec Travaux Sci Med Congo Belge* Léopoldville 1944 Jan. No 2 162-4

This short note on leprosy prevalence among the pygmy tribes of the Belgian Congo raises the question as to how far neural types of leprosy may be contagious to the healthy. The author's experience has led him to admit the occurrence of new infections in areas with only neural cases or with only vague evidence of the presence of lepromatous patients. He admits that he is dependent on the accuracy of his informants but the examination of a number of pygmies confirmed his hypothesis and he gives data of a number of villages in which only neural cases were found mostly of a very mild type. He points out that nerve cases may at times show lepra bacilli in their nasal cavities which are likely to be infective. In the Nepoko area 5 to 6 per cent of the population are infected and out patient treatment is the method of choice for most cases but those with lepra bacilli in the nasal secretions are better isolated.

DAVISON A R Decolorizing of *Mycobacterium leprae* *Internat J Leprosy* Cleveland Ohio. 1943 Dec. v 11 49-51

In nerve leprosy incision and scraping of the perineurium of thickened nerves almost invariably reveals bacilli, a scraping of the nasal mucosa may do so but an incision of a macule rarely does. In 80 per cent of these cases lepra bacilli are not found and diagnosis must therefore be made without by other means. The laboratory technique for staining is not standardized and presents pitfalls. The author has found inadequate the recommended method of staining with fuchsin for two minutes with the same period of time for decolorizing in a 5 per cent sulphuric acid and for staining with methylene blue. He advises staining for five minutes in warm fuchsin decolorizing for 20 minutes in 5 per cent sulphuric acid and counterstaining for two minutes with methylene blue. Otherwise diphtheroids are liable to be mistaken for Hansen's bacillus.

PARMAKSON P Die pathohistologische Reaktion der Haut bei Lepra. [The Pathological Reaction of the Skin in Leprosy] *Deut Tropenmed Ztschr* 1943 Nov 1 v 47 No 21/22 545-77 10 figs [45 refs.]

The author reports the results of a careful study of 20 lepromatous and 18 nerve leprosy cases in different stages of the disease by means of microscopic

sections of the affected skin (including examination for *M. leprae*) the sedimentation test and the Mitsuda reaction. The most important data are shown in a table and the answers to five questions he set himself to deal with are as follows:

- 1 Active skin lesions of nerve leprosy are characterized by tuberculoid changes.
- 2 In the case of clinically lepromatous lesions the morbid histology shows no tuberculoid changes in the skin.
- 3 In clinical nerve cases no lepromatous changes are found on section.
- 4 Tuberculoid and lepromatous changes do not appear simultaneously.
- 5 It is improbable that a change from one type to the other could be followed histologically. The typical changes of one type disappear before those of another type appear.

The data recorded regarding the red cell sedimentation rate are in accordance with those of other observers in that it is increased in well-marked lepromatous cases, although this may not be so in early cases. Nerve cases show increased rates only when complications are present such as perforating ulcer of the foot. The Mitsuda reaction was negative in nearly all lepromatous cases except those in a very early stage and positive in nerve cases as found by others. [The histological changes are well illustrated and the paper is worthy of close study by those interested.]

L. Rogers

SLOAN N. R. Early Diagnosis of Leprosy as seen in Hawaii. *Hawaii Med J* 1944 Jan.-Feb. v 3 No 3 111-20 4 figs.

The first part of this paper deals with the subject generally and the author is in agreement with medical opinion regarding transmission and race sex and age incidence. He commences by claiming that compulsory segregation is effective in Hawaii, and that the decline in known active lepers from 1 175 in 1890 to 390 in 1943 is evidence of this. A careful analysis is given of the symptoms in 743 cases which shows the following frequency of the more common symptoms:—Macules (spots and blotches) 344 nodules 97 anaesthesia 64 ulcers 63 swelling of skin 44 muscular weakness 31 contracture of fingers 28 erythema 17 etc. The early symptoms are then described on the usual lines and the methods of examination given. These will be useful to those without much experience of the disease.

L. Rogers

PEIKOTO P. G. Leprosy and Syphilis. *Internat J Leprosy* Cleveland Ohio 1943 Dec. v 11 43-8 6 figs on 2 pls.

This is the report of a case in which the diagnosis between leprosy and syphilis was difficult: the patient was a negro in Brazil, who had never lived with a leprosy patient and denied having had syphilis. A number of somewhat infiltrated, lighter-coloured patches were present on the face, body and limbs with some loss of sensation to heat and pain but not to touch: there was no thickening of nerves. No lepra bacilli were found in the nose or in a gland. The histamine test showed lack of the second erythema on all the lesions and microscopically the giant cells of Langhans were found in a few places. Wassermann and Müller blood tests were positive and neosyphenamine treatment produced considerable improvement in the skin lesions without modifying the loss of sensitivity. It was therefore concluded that the case was one of mixed leprosy and syphilitic origin.

L. Rogers

FERNANDEZ J M M Sensitization to Lepromin in presumably Non-Leprous Individuals. *Internat J Leprosy* Cleveland Ohio 1943 Dec. v 11 15-22. [12 refs.]

After reference to the late reaction produced by Mitsuda's method which is here called integral lepromin and the early reaction induced by injection of the protein fraction of *M. leprae* the writer reports the results of his studies of the sensitizing action of integral lepromin and of suspensions in mineral oil of Hansen's bacilli killed by heat of the tubercle bacillus killed by heat and of the typhoid bacillus. He reports that presumably non-leprous subjects can be sensitized to lepromin by intradermal injection of an oily or aqueous suspension of *M. leprae* killed by heat and by suspensions of killed tubercle bacilli. He also found the early lepromin reaction to be attributable to previous sensitization induced by either lepra or tubercle bacilli. On the other hand sensitization to lepromin was not induced by previous intradermal injection of purified lepromin protein (L.P.P.) or of suspensions of killed typhoid bacilli. The duration of sensitivity to lepromin is not yet established but it has persisted as long as five years after intradermal injections of integral lepromin. It has not yet proved possible to provoke a supposedly protective allergy since it is apparently dependent on an unknown factor which may be constitutional.

L Rogers

ROSS Hilary Euglobulin in Leprosy. *Internat J Leprosy* Cleveland Ohio 1943 Dec. v 11 23-6 [10 refs.]

Estimation of the total proteins albumin globulin and euglobulin have been made in 150 cases of leprosy of various types and stages. The methods used are described and the euglobulin tyrosin indices are given. In 147 cases the index was above normal, and of these the albumin-globulin ratio was below normal in 123 and in the rest it was normal. Higher tyrosin indices were met with in active and moderately or far advanced cases. It is suggested that hepatic dysfunction and liver damage may be the aetiological factor in the changes noted.

L Rogers

ECCLES C G & ROSS Hilary The Mazzini Flocculation Slide Test compared with the Kolmer-Wassermann and Kahn Standard Tests in Leprosy. *Internat J Leprosy* Cleveland Ohio 1943 Dec. v 11 27-31 3 figs.

The authors refer to the results obtained by MAZZINI [see RATCLIFFE *Bulletin of Hygiene* 1940 v 15 716] with his flocculation slide test with the serum of 60 leprosy donors referred to at the Washington Serology Conference of 1941 [*ibid* 1942 v 17 849]. Of these only 17.2 per cent were positive against 54.2 per cent with Kolmer's simplified complement fixation test and 59.6 per cent with the Kahn standard test. The Mazzini test has the advantages of economy of time and materials and ease of preparing the reagents. The present authors record results on 142 sera in which there were fewer positive results with the Mazzini test (with 28.9 per cent.) than with the Kolmer and Kahn tests (33.8 and 39.4 per cent. respectively) but the Mazzini test showed 16.9 per cent. doubtful reactions against 11.2 and 4.4 per cent with the other two tests respectively. On account of its greater simplicity the Mazzini test should be of special value for use in mobile laboratories and in small or isolated leproseries.

L Rogers

FAGET G H & FOGGE R C Pooled Blood Plasma Transfusions in the Treatment of Leprosy. *Internat J Leprosy* Cleveland, Ohio 1943 Dec. v 11 32-5

Although certain forms of serum treatment of leprosy have been advocated the use of normal human serum or plasma has not been given a fair trial in

economic loss and are refractory to treatment. They and *A. muris* live in a similar environment in the small intestine. The apparatus used is figured and described. Mortality of the nematodes was estimated by removing the piece of gut perfused to aerated Tyrode-glucose solution at 38°C. scraping the mucosa with a blunt scalpel and transferring the nematodes, thus set free, to Tyrode-glucose solution saturated with 95 per cent. O_2 , 5 per cent. CO_2 gas mixture at 40°C. in a counting dish. After half a minute the proportion of active worms was determined over a period of 4 minutes. The same examination was done after incubation of the parasites in saline for 1 hour. The accuracy of this method was confirmed by killing known numbers of nematodes by heat or 1/1 000 carbon tetrachloride in saline, and mixing these with known numbers of living nematodes incubated in saline for two hours.

The effects of mucus on drug efficiency were studied by examining separately after perfusion the nematodes free in the gut lumen and those which had to be scraped from the mucosa, i.e. which were under the mucus. Trim (*loc. cit.*) showed that gastric mucus inhibits the action of hexylresorcinol. Anthelmintics may by the irritation they cause induce mucus secretion. The amount of mucus per unit area and unit weight of small intestine before and after perfusion was therefore determined to find out the effect of hexylresorcinol and tetrachlorethylene on mucus secretion. Because perfusion tended to loosen the mucus round the nematodes the drug penetration observed was probably much better than can be expected under natural conditions. It was found by preliminary perfusions by X-ray examination of the passage of a barium meal and by experiments on the rate of passage of hexylresorcinol along the alimentary canal, that a perfusion time of 2 hours was the most reasonable.

The effect of anthelmintics was greater on nematodes free in the gut lumen than on those attached to the mucosa. A concentration of 1/2,000 hexylresorcinol was most active in the presence of 0.2 per cent. sodium oleate probably because of the surface activation caused but the soap itself showed a rapidly increasing anthelmintic activity in concentrations above 0.2 per cent. Similarly 1/2,000 hexylresorcinol in the presence of 0.125 per cent. of sodium laurate inactivated 100 per cent. of the nematodes and in the presence of 0.031 per cent. of sodium laurate 90 per cent. were inactivated, probably because the soap itself was anthelmintic. 0.5 per cent. of it killing almost all the nematodes rendering them almost colourless with maturation of their tumes. Tetrachlorethylene on the other hand, was not markedly affected by sodium oleate. The addition of 0.03 per cent. sodium taurocholate increased the anthelmintic action of 1/2,000 hexylresorcinol, 70 per cent. of the nematodes being then inactivated, but decreased it when 0.25 per cent. or higher concentrations of bile salt were used. High concentrations of bile salt removed the gut mucus. Tetrachlorethylene in moderate concentrations was not greatly affected by bile salts. Ascorbic acid had little effect on the action of hexylresorcinol. For the *in vivo* tests of anthelmintic action the egg counts done before treatment were used to predict the number of nematodes expected to be present before dosing. The results showed that 115 mgm/kgm hexylresorcinol, i.e. one-fifth of the L.D. 50 dose (see LAMBOY BROWN and WARD *J. Pharmacol. & Exper. Therap.* 1935 v. 53 568-575) did not apparently affect the nematodes because 98 per cent. of them survived. When one-quarter of the L.D. 50 dose was perfused, 94 per cent. survived. But with even only a very small dose of tetrachlorethylene (1 cc./kgm.) only 20 per cent. of the nematodes survived, and the efficiency of 0.1 cc. of it was not impaired by the addition of 20 mgm. of sodium taurocholate.

The bulk of the nematodes were found in about 15 cm. of the small intestine about 20 cm. from the pylorus. Dosing caused them to move down the intestine although their position was not greatly affected by tetrachlorethylene. Hyperperistalsis induced by increasing the osmotic pressure of the medium in the

bath in which the perfused gut was studied (the apparatus enabled kymographic records of the intestinal movements to be made) did not displace the nematodes, although large volumes of fluid perfused loosened the mucus. But tetrachlorethylene freed the parasites from mucus or stimulated them to enter the gut lumen where many were killed. Not all nematodes killed by hexylresorcinol or tetrachlorethylene were passed immediately—some remained *in situ* and were digested 4 hours later.

The movement of the parasites down the gut was used to study the rate of action and relative activity of the two anthelmintics used. It was confirmed that hexylresorcinol is inactive against *N. muris* in the rat. The *in vitro* tests had suggested that it was inhibited by bile salts by the rate of its passage down the gut or by its rate of passage through mucin. These three factors were further studied. It was found that when they gained contact with the nematodes both hexylresorcinol and tetrachlorethylene probably acted rapidly. The fall in the killing rate after longer periods seemed to be due to the protection afforded by the mucus. In concentrated doses tetrachlorethylene acted rapidly—many worms being killed by it within one hour. This drug moved down the gut at a rate similar to that of a water barium meal and was often found 60 cm from the pylorus after two hours. Thus anthelmintics must kill rapidly and at low concentrations to be effective in the short active gut of the rat. Phenothiazine for example which acts slowly and is efficient only in high concentrations cannot affect *N. muris* unless its killing rate is artificially increased or its passage down the gut is delayed. Effective concentrations of it pass through the rat gut in one hour while they require six hours to pass through the sheep gut.

Trim showed that 1 per cent. sodium taurocholate completely inhibits the passage of hexylresorcinol through the cuticle of *Ascaris lumbricoides*. Rogers found that 1 per cent. sodium taurocholate reduced the efficiency of hexylresorcinol against *N. muris* by 50 per cent. It was found that the concentration of taurocholate in the intestine of the rat varied from 0.6 to 1.3 per cent. half an hour after the dosing with hexylresorcinol. These figures may be low because infested rats seem to pass more bile salt and ether which depresses bile secretion was used during the dosing and for killing. With larger doses the figures may be high because the soaps and resorcinol stimulate hepatic secretion. It was therefore concluded that the therapeutic dose of hexylresorcinol and sodium oleate may be inhibited 50 per cent. by bile salt. Adsorption of hexylresorcinol on to mucus reduces its concentration in the gut fluids and also prevents its penetration to the parasites in the mucus. These factors account for the inefficiency of hexylresorcinol against *N. muris*.

Trim found that low concentrations of sodium oleate increased the rate of penetration of hexylresorcinol through the cuticle of *Ascaris lumbricoides*. Rogers found that this also happens with *N. muris* but at concentrations of 0.2 to 1 per cent. of sodium oleate hexylresorcinol was inhibited and at concentrations of 1 per cent. and upwards the soap alone killed the *N. muris*. Sodium laurate activated hexylresorcinol more effectively than did sodium oleate at pH 6.5 and this soap also had an anthelmintic action but at lower pH levels the activity levels of oleate and laurate are reversed so that in alkaline media oleate may be the more efficient against the nematodes.

The protective action of mucus was evident even though the perfusion loosened the mucus. Not only did the parasites seem to stimulate the secretion of mucus but they were also found deep in mucus between the villi so that they were well protected. Adsorption of hexylresorcinol on to mucus first occurred in the stomach and the small amounts reaching the small intestine were further reduced by adsorption on to the mucus there. The concentration of hexylresorcinol in the small intestine therefore probably only rarely reached levels

toxic to the nematodes. Additional causes of the drug's failure were its inability to perfuse through the mucus to the parasites and its poor ability to penetrate through the nematode cuticle demonstrated by Trim. Its anthelmintic efficiency might be increased by (1) reducing its adsorption on to mucus e.g., by giving it with an enteric coating insoluble in the stomach (2) reducing gastric and duodenal mucus with atropine (3) lowering mucus viscosity (ascorbic acid failed to do this in the author's experiments) (4) withholding food, which also adsorbs hexylresorcinol and stimulates the secretion of the inhibitory bile and mucus. The success of hexylresorcinol against other nematodes may be due to the ingestion by these parasites of mucus with hexylresorcinol adsorbed on to it. Brown [this Bulletin 1933 v 30 696] recorded for example the failure of hexylresorcinol against *Euderobius vermicularis* when it was given by the mouth. It probably failed for the reasons given above. But when it was given by enema and the inhibitory factors studied by Rogers and Trim were avoided, it succeeded.

The wide range of activity of tetrachlorethylene may be due to its relative therapeutic stability in gastric and intestinal fluids and to the fact that bile and mucus have little effect on it.

The anthelmintic action of detergents similar to the sodium oleate and laurate used by Rogers should be further studied. G Lapage.

OLIVER O W. Bionomics of the Lynceid Snail, *Stagnicola palumoides teckella*, the Intermediate Host of the Liver Fluke in Southern Texas. *J Agric. Res.* 1944 Nov 15 v 69 No. 10 388-403 4 figs. [24 refs.]

BAYLIS, H. A. Tapeworm in Trout. [Correspondence.] *Brit Med J* 1944 Dec. 30 868.

The author refers to the reports of DUGUID & SHEPPARD [this Bulletin 1944 v 41 857] HICKEY & HARRIS (*ibid.*, 858) UNSWORTH (*Brit Med J* 1944 Sept. 16 335) and HICKEY (*ibid.* Oct. 7 482). He has examined specimens sent to him by all these workers and concludes that those from gulls were of one species and those from the cormorant were of another species. On comparing adult worms obtained experimentally in mammalian hosts by all the workers, he found that they all strongly resembled Hickey's species from gulls and concludes that the experimenters were dealing with a single form, very probably an old but little-known species *Diphyllobothrium dendriticum* (Nitzsch 1824) normally a parasite of gulls. Slight differences might be the result of development in abnormal hosts (mammals). J F Corson.

ADDIS, C. J. & CHANDLER, A. C. Studies on the Vitamin Requirement of Tapeworms. *J Parasitology* 1944 Aug v 30 No. 4 229-36.

Little work has been done on the vitamin requirements of cestodes. HAGER ANDER [*Iowa State Coll. J. Sci.* 1941 v 15 127-153] found marked decrease in the egg production of *Hymenolepis diminuta* in rats kept on a diet deficient in vitamin "G-complex," but not when vitamin B₂ was deficient. CHANDLER [this Bulletin 1943 40 705] found that *H. diminuta* is totally independent of the protein in the diet of the host and concluded that these cestodes obtained their protein by absorption direct from the host's mucosa and that this might explain the stunting of their growth by crowding. He also found that lack of vitamins in the host's diet, with or without the provision of protein, markedly affected the establishment of the worms in female rats but not in male rats. For this reason the work here recorded was done with female rats only. Chandler's further work showed that this cestode is dependent on some factor

in autoclaved yeast in the host's diet but that lack of the fat-soluble vitamins A D E and of vitamin B₁ had no effect on the growth of the worms in female rats

For the present investigation the method used in the author's earlier work was employed. Groups of female rats were taken and each rat was given 10 cysticercoids reared by infection of the grain beetle *Tenebrio molitor*. Rats were autopsied 14 days after infection because then no segments are yet shed although the cestodes have an average length as great as the length they attain later on. Details of the diets of the rats are given.

Experiment showed that lack of vitamins has some effect on the ability of the cestodes to establish themselves and on their growth even when the host's vitamin reserves are intact i.e. when the rats are put on deficient diets on the day on which they are infected. In experiment 2 the rats were allowed four days in which to use their vitamin reserves before they were infected. The result was that the number and size of the cestodes in the rats on deficient diets were reduced still further. The greatest stunting of the worms occurred in the groups lacking either all vitamins or only G-complex [riboflavin]. Lack of vitamins also definitely decreased the number of worms that established themselves.

In experiment 3 the rats were allowed 17 days in which to deplete their vitamin reserves before they were infected. The results showed that the effects of lack of vitamins were intensified. In the group whose diet was deficient in G-complex marked stunting of the cestodes occurred while in groups getting adequate G-complex the cestodes grew longer than they did in the controls. This confirmed the view that these cestodes need for their normal growth enough G-complex. The results also indicated that without vitamins A D E and B₁ the cestodes grow larger rather than smaller. Absence of G-complex and of vitamins A D and E also intensifies the reduction of the number of cestodes which establish themselves but absence of B₁ does not. Thus *H. diminuta* is dependent on G-complex in the host's diet. It is suggested that the cestode obtains it from the host's mucosa. The author is studying what components of the G-complex are concerned in this effect. Since the worms grow in a perfectly normal manner in the absence from the host's diet of any vitamin except something associated with the G-complex even after the host has depleted its vitamin reserves for a long period (17 days) it is suggested that the cestodes synthesize these vitamins. The increase in the size of the cestodes in rats on diets deficient in fat-soluble vitamins agrees with the work of ACKERT, McILVAINE and CRAWFORD (*Amer J Hyg* 1931 v 13 320-336) who found an increase in size of the nematode *Ascaridia lineata* in chickens on a diet deficient in vitamin A and attributed it to partial paralysis of the intestine and consequent richer flora in the intestine. This partial paralysis would allow *H. diminuta* to take up a more anterior position in the intestine which would be more favourable to its growth (cf. the work of BURLINGAME and CHANDLER *Amer J Hyg* 1941 Sect D v 33 1-21 on *Moniliformis dubius* of the rat) and this would explain why the cestodes grew to a greater size in the vitamin-deficient rats than in the controls.

The establishment of the cestodes in the gut seems to depend on proper evagination of the scolices and on their successful attachment. Evagination probably depends on the digestive juices and the pH and EDGAR (1941 *Trans Amer Microscop Soc* 1941 v 60 121-123) suggests that proper secretion of bile would be necessary for evagination. [The toxicity of sodium glycocholate to scolices of *Taenia hydatigena* is discussed by DE WAELE (*Ann Parasit Humains et Comparés* 1934 v 12 492)] Possibly lack of vitamin A interferes with normal bile secretion and if so scolices might evaginate only near the entrance of the bile duct and the others would be carried away. G. Lapage

[April 1945]

Tropical Diseases Bulletin

WHITELAW J. C. G. & SANDY P. A Case of Infection of a European with *Strongyloides stercoralis*. *J. Roy Army Med. Corps.* 1945 Jan., v 64 No. 1 35

SCHUBERT R. Askanden-Cholangitis und Pankreatitis. (Cholangitis and Pancreatitis due to *Ascaris*) *Med. Klin.* 1943, Jan. 16 v 39 No. 2, 34-7 1 fig [Numerous refs.]

KING B. G. Early Filariasis Diagnosis and Clinical Findings: a Report of 299 Cases in American Troops. *Amer. J. Trop. Med.* 1944 Sept. v 24 No 3 285-98 1 fig [28 refs.]

[WARTMAN and KING (this Bulletin 1944 v 41 880) published an abstract of this paper and the succeeding one (WARTMAN below) before they appeared. The present papers give more detailed accounts.]

Clinical observations were made on 288 American soldiers who showed symptoms of filariasis after exposure to possible infection in Pacific islands during the period from May to September 1942. The author first saw them in January 1943.

Incubation period.—The earliest onset of symptoms was three months after arrival in the islands. A graph shows that in about 60 cases the incubation period was from 3 to 9 months, and in about 200 it varied from 10 to 18 months.

Mode of onset.—Only two patients had fever and headache at the onset. The first symptoms were pain, swelling or redness of an arm or leg or pain and swelling in the scrotal region. The pain was never severe in the limbs and only rarely so in the scrotal region.

Clinical symptoms.—No cases of arthritis, hip-joint abscess, varicose glands or elephantiasis were observed. Fever occurred in 19.7 per cent and was nearly always mild and lasted for a few days only. The syndromes could be classified in three groups: lymphangitis of the trunk or extremities, acute inflammation of the scrotum or its contents, and enlargement of lymph nodes. Relapses were frequent—one patient had lymphangitis six times—but acute local symptoms usually lasted for a few days only. No patient was seriously ill but working efficiency was much interfered with.

Lymphangitis.—This was present in 51 per cent and occurred most frequently in the arm. It took three forms—red streaks, patches of subcutaneous oedema and overlying redness or diffuse oedema and erythema. As others have stated it tended to extend centrifugally.

Genital lesions.—Inflammation of the spermatic cord, epididymis, testis or scrotum occurred in 71.6 per cent. Funiculitis and epididymitis were the most frequent. The pain was sometimes exquisite.

Lymphadenopathy.—As others have noted this was most frequent in the epitrochlear glands.

The blood showed eosinophilia in about two-thirds of the patients. One-quarter of them however had intestinal worms chiefly *Necator americanus* and *Trichuris trichiura*. There was no leucocytosis. Microfilariae were not found in the blood though carefully looked for.

Diagnosis.—The author thinks that a clinical diagnosis is reliable. Lymphangitis may be mistaken for thrombophlebitis, epididymitis for gonorrhoea and funiculitis for hernia. The intradermal test described by TALLAFERRO and HOFFMAN [see this Bulletin 1931 v 29 214] and by FAIRLEY (ibid., p. 879) was used. Two antigens were made but one was found to be much more reliable than the other. It gave a positive reaction in 90.8 per cent. of the patients and in 10.5 per cent. of the controls. The author got strong evidence that positive

reactions were not produced by intestinal worms. From direct and indirect evidence he concludes that the patients were suffering from filariasis due to *Wuchereria bancrofti* J F Corson

WARTMAN W B Lesions of the Lymphatic System in Early Filariasis *Amer J Trop Med* 1944 Sept v 24 No 5 299-313 20 figs [16 refs.]

This paper deals with material removed by biopsy from some of the cases of filariasis reported on by KING [above]. The material consisted of 20 lymph nodes and 4 cord like structures from lesions of acute lymphangitis removed from 17 soldiers. They had been exposed to infection for about four months in certain Pacific islands followed by five months in the Solomon Islands. It is very probable that they became infected during the former period. The specimens were eight epitrochlear, six axillary and six inguinal lymph nodes, three cords from the epitrochlear region and one from the axilla. Aerobic and anaerobic cultures from these specimens were negative. Semi-serial paraffin sections were examined and the findings are given in detail in a table and illustrated by photomicrographs. Adult male and female filarial worms were found in five specimens.

The lymphatic glands and vessels showed granulomatous inflammation around the worms in the lymphatic sinuses and in the capsule; these changes are described and figured. The worms were within enormously dilated cortical and medullary sinuses and were surrounded by macrophages and reticular cells with eosinophils and giant cells of the foreign body type. The lesions of the lymphatic vessels included proliferation of the endothelium and of the reticular cells, acute lymphangitis with or without thrombosis and fibrous obliteration. Some worms were apparently alive at the time of biopsy and the tissue reactions around them were the same as those around dead worms. No free microfilariae were found. The author refers to a special article [this *Bulletin* 1944 v 41 800] which was an abstract of KING's paper [above] and this one and to papers by FLYNN [this *Bulletin* 1944 v 41 956], MICHAEL [*ibid*] and HARTZ [*ibid* 955] as well as to earlier well known publications on this subject J F Corson

BINGHAM J A W & McDONALD S A Filarial Nodule simulating a Cyst of the External Semilunar Cartilage *Brit J Surgery* 1944 Oct v 32 No 126 326-7 1 fig

A cyst of *Onchocerca volvulus* situated on the outer side of the left knee of a West African soldier serving in India, was excised in mistake for a cyst of the external semilunar cartilage. It was found to lie between the capsule of the joint and the synovial membrane, exactly opposite the joint line in the middle of the outer side. The nature of the cyst was not suspected until paraffin sections were examined, though the species of filaria was not identified from the sections; there could be little doubt that it was *Onchocerca volvulus*. [Biopsy of the skin might have suggested or confirmed the diagnosis. see this *Bulletin* 1923 v 20 945 1924 v 21 214] J F Corson

TALICE R V Estudios sobre la triquinosis. III. Cuando debe el médico pensar en la triquinosis? [Studies in Trichiniasis. III. When should the Physician think of Trichiniasis?] *Arch Uruguayos de Med Cirug y Especialidades* 1944 Sept v 25 No 3 237-43 English summary

There is not a typical and uniform picture in trichinosis; only exceptionally does the physician encounter a really typical case of the disease; the patients show signs of very variable localisation.

In the epidemic cases—whether great or small epidemic—the clinical diagnosis can be traced on epidemiological basis (ingestion of pork flesh) and the presence of common symptoms (especially oedemas of the face or other parts of the body muscular pains diaphragmatic signs, fever, loss of weight, digestive, hepatic and gastric signs blood eosinophilia, etc.)

"In the sporadic cases and on account of the endemic features of trichinosis in Uruguay particularly in the rural zones the physicians must think of that disease in all cases with high blood eosinophilia, oedemas, muscular pains apparently allergic symptoms or diaphragmatic signs (pseudo-hepatic pseudo-pneumonic, etc.) in the right side.

The confirmatory diagnosis can be made only by laboratory methods and in specially trained services. In a next article I shall present a critical review about this aspect of the problem.

WRIGHT W. H. JACOBS L. & WALTON A. C. Studies on Trichinosis. XVI. Epidemiological Considerations based on the Examination for Trichinae of 5,318 Diaphragma from 189 Hospitals in 37 States and the District of Columbia. *Pub Health Rep Wash.* 1944, May 28, v 59 No. 21 669-81

This paper is reviewed in *Bulletin of Hygiene* 1945 v 20 16.

HORNE, S. F. & HARRELL, G. T. Trichinella Skin Tests in Patients in General Hospitals and Tuberculosis Sanatoria. *Amer J Med. Sci.* 1944 June, v 207 No. 6, 759-65.

This paper is reviewed in *Bulletin of Hygiene* 1945 v 20 17

DEFICIENCY DISEASES

1. TROWELL, H. C. Malnutrition in the Bantu of Central Africa. A Syndrome of Malignant Malnutrition. *Clin Proc Cape Town* 1944 Oct v 3 No 8 381-401 10 figs. [14 refs.]
2. BROWN J. SCOTT & TROWELL, H. C. Deficiency Bowel Pattern in Polish Refugees, African and Indian Adults and Children (Kwashiorkor). *Lancet* 1944 Dec 23, 812-16 2 figs.

1. In both articles will be found descriptions of the now well-known syndrome which in the past has been known as infantile pellagra but which subsequently was shown to occur in adolescents and adults. These accounts differ in no essential details from those already given by Trowell and others previously. The first article makes a most readable narrative and needs no further discussion except in regard to nomenclature. Trowell says "unfortunately it is necessary to call the syndrome by a certain name, or it will be seldom diagnosed and treated. Such are the limitations of the human mind. He therefore calls it "the syndrome of malignant malnutrition. [His strictures on the limitations of the human mind are not perhaps without foundation it is only necessary to recall the confusion which has arisen in vitamin nomenclature and which has occurred concerning some of the conditions ascribed to vitamin deficiencies. We like labels they are useful but would it not be wiser to wait till the pathogeny of the many deficiency syndromes has been worked out before attempting to give specific names to them. The expression "The syndrome of malignant malnutrition," it is suggested, is an unfortunate one—it is a title which surely should be claimed by pellagra, if for an instant the mortality of that disease, as it occurred last century in Italy and later in the endemic areas of U.S.A. be recalled].

The facts in regard to the condition under discussion appear to suggest a deficiency of calories of protein and of vitamin B complex including nicotinic acid and riboflavin other factors in causation being helminthic and protozoal infections. [It is not clear, however why the few develop the syndrome while others escape.]

ii In the second paper the results are given of radiological examination of the gastro-intestinal tract, after the method of GOLDEN in U.S.A. (*Radiology* 1941 v 36 262 *J Amer Med Ass*, 1941 v 117 913) in 16 cases comprising 2 Polish refugees a nan an Indian 10 African labourers all of whom had suffered dietary deficiency with a variety of symptoms and 2 African children with symptoms of infantile pellagra.

The observations were mainly screen examinations. The appearances found were similar to those described by Golden and called by him the deficiency pattern but it was not seen in every case of gross deficiency state. [The authors apparently accept Golden's explanation of the pattern without comment but it should be pointed out that the theory he put forward has been criticized by other workers.]

H S Stannus

SPIES T D COGSWELL R. C & VILTNER, C. Detection and Treatment of Severe Atypical Deficiency Disease *J Amer Med Ass* 1944 Nov 18 v 126 No 12, 752-8 4 figs

The authors point out how much the pattern of the symptoms in nutritive failure may vary and how difficult it may be for the practising physician to recognize these patterns.

Ten cases are then recorded to illustrate the point including (1) A negro child, aged 5 months who after a severe infection (pneumonia) suddenly developed a watery diarrhoea and fiery red tongue symptoms which responded to nicotinic acid in four hours. [It is not mentioned whether the child had received any sulphonamide drug.] (2) A white female aged 33 with a history of restricted diet associated with mental depression but no stigmata of vitamin deficiency who recovered rapidly with the exhibition of nicotinic acid. (3) A 67 year-old white female complaining of intense burning pain in the soles of the feet associated with an ill balanced diet which responded to an intravenous injection of 100 mgm. of thiamin. (4) A white male aged 63 with pain in one eye and failure of vision associated with loss of weight dizziness weakness and nervous depression. The affected eye was injected and a small corneal ulcer was present. [Corneal vascularization is not mentioned presumably a slit-lamp examination was not made.] All the symptoms cleared up with riboflavin 20 mgm. intravenously daily for two weeks. (5) A case showing sore mouth and tongue associated with diarrhoea mental confusion and burning feet each year in spring and autumn which responded to thiamin etc. [Such cases one believes are commoner in Britain than is usually suspected. The occurrence of the syndromes of odd pattern should always be present in one's mind when investigating cases with a history of restricted diet or possible failure of absorption.]

H S Stannus

REMINGTON R. E. The Enigma of Pellagra. *Southern Med J* 1944 Nov v 37 No 11 605-14 7 figs

The author says the study of mortality and morbidity statistics [for pellagra] over a period of years reveals a number of facts which are difficult to interpret in the light of present day knowledge. Some of these are presented and discussed. They relate entirely to the endemic area in the cotton belt of the Southern States.

The author points out how when the statistical data are broken down the original interpretation may be found to be misleading. There was a decline of 77 per cent. in pellagra mortality rates in 13 Southern States between 1928 and 1940. In South Carolina, where the death rate was higher than in any other area, the decline has continued through 1943 amounting to 91 per cent. of the rate in 1928 with a parallel drop in the incidence of the disease. This the author shows, is due to some cause or combination of causes which affects the entire population, and not to remedial measures. Relief measures in the form of money or food in 1935 to 1938 had no effect.

The mortality among negroes is higher than among the whites but has decreased more rapidly—the means by which this population fraction, of the lowest economic status has been able to make superior progress in eradicating pellagra is not clear but possible explanations are suggested. It appears possible that some set of circumstances may have forced the population to produce or obtain by other means a greater variety of foodstuffs.

Attention is drawn to the difference between the sexes—the death rate in female negroes is 2.5 times as great as that in male negroes—in female whites 1.75 times as great as that in male whites.

The article is an interesting contribution to the epidemiology of pellagra.

H. S. STANNUS

FINNERUD C. W. *Peribehn*—its Nosologic Status. *J Amer Med Ass.* 1944 Nov 18 v 126 No. 12, 737–40. [31 refs.]

A discussion upon the several conditions due to a variety of causes which the author considers may be grouped together under the term "*peribehn*" and which he seems to believe cannot be diagnosed the one from the other.

[Finnerud fails to realize that the term was invented for a specific condition due to a specific cause. Presumably therefore it should not be used in a wider sense. The subject has already been dealt with in Britain by the reviewer who puts in a plea that this foreign word should be suppressed. *Practitioner* 1941 v 146 303. *Brit Med J* 1944 July 29 140. *Lancet* 1945 Feb 3 161.]

H. S. STANNUS

PETRI, S., NORGÅRD F. & KJÆR, W. Studies on the Causation of Experimental Gastrointestinal Pellagra. IV. Therapeutic Experiments on Pig with Preventive Parenteral Administration of Vitamin B₃. *Acta Med. Scandinavica* 1944 v 119 No 4–5 356–63 5 figs. [10 refs.]

SEVRENGHAUS E. L. Adult Needs of Vitamins A and C. *J Amer Med Ass* 1944 Nov 18 v 126 No 12, 751–2.

The author believes that many individuals in the United States are not receiving a sufficiency of vitamins A and C and refers to the difference in opinion as to optimum amounts per day. He thinks 15 mgm. of ascorbic acid and 5 000 I.U. of vitamin A approximately correct.

H. S. STANNUS

HAEMATOLOGY

BROCK, J. F. Recent Advances in the Aetiology, Terminology and Classification of Anaemias. *East African Med J* 1944 Oct. v 21 No 10 298–309 1 fig. [21 refs.]

This communication is an account of an address given before the Kenya Branch of the British Medical Association.

It comprises a survey of some recent views on the classification of anaemias on the basis of aetiology, together with a description of modern methods of studying the morphology of the peripheral blood in the diagnosis of anaemic states. Especial reference is made to recent work on tropical nutritional anaemias.

In the course of a preliminary consideration of normal haemoglobin levels and of the effect upon them of residence at high altitudes the author states that iron therapy has a stimulating effect on erythropoiesis which is independent of its action in correcting deficiency. He argues consequently that conclusions based upon mass haemoglobin surveys may be fallacious if the demonstration of the apparently sub-normal haemoglobin levels which are found to rise after the administration of iron be interpreted as necessarily indicating a pre-existing state of anaemia.

L. J. Davis

VENOMS AND ANTIVENENES

BOGNET P. Recherches sur le venin de *Dendraspis viridis* [On the Venom of *Dendraspis viridis*] *Bull. Soc. Path. Exot.* 1943 May 12 & June 9 v 36 Nos. 5-6 189-90

The author has studied two specimens of dried venom from *Dendraspis viridis* sent from Kindia (French Guinea). They were light yellow in colour and readily soluble in saline. The results of his investigations were —

Specimen I — A rabbit of 2,500 gm. injected with 1 mgm. (0.8 mgm. per kilo body weight) shows progressive paralysis and death in asphyxia in 1½ hours. Guinea-pigs are less susceptible. Intravenous injection of 0.5 mgm. into an animal of 350 gm. (1.45 mgm. per kilo) causes death in 15-20 minutes while 1 mgm. subcutaneously kills in about 10 hours. Smaller doses than this have no effect. Mice of 18-20 gm. die within an hour of intraperitoneal injection of 0.1 mgm. At autopsy congestive perhaps haemorrhagic foci are found in the intestine.

Specimen II — This proved to be more toxic, says the author, but his records hardly bear this out. The difference was very slight. Intravenously 0.7 mgm. per kilo killed a rabbit and 0.1 mgm. killed a guinea-pig of 350 gm. and 1 mgm. subcutaneously was fatal to the latter animal (so was specimen I).

Attempts to neutralize the venom with antivenenes of *Naja tripudians*, *N. haje*, *Vipera aspis* and *Bilis arctans* were ineffectual. The action of the venom is thus like those of other African Colubridae, but is less powerful. Antivenenes for bites by Equatorial and West African snakes should therefore contain that for *Dendraspis* also as its antigenic properties are specific.

MADAME PHISALIX in the discussion on this paper showed how the fangs of *Dendraspis* are long and demonstrated with the skull of *D. jamesoni* that they are so disposed that the venom is introduced under pressure like a dagger thrust, into the depths of the tissues and that the elasticity of the tissues closes up the path of the fangs and the venom thus gains access rapidly to the bloodstream and symptoms begin to appear very soon after the bite.

H. Harold Scott

LINHARES H. Variações da pressão arterial e líquorica após inoculação de peçonhas de jararaca e cascavel [Variations in Arterial Blood pressure and in the Cerebrospinal Fluid after Inoculation with Crotaline and Bothrops Venoms.] Reprinted from *Jornal dos Clinicos* Rio de Janeiro 1938 Oct 30 No 20 8 pp.

The author was desirous of finding out whether the results of the blood and spinal fluid pressures were the same after inoculation of the venoms of *Crotalus*

and *Bothrops* as Koresnos had reported with that of *Naja tripudians*. Koresnos had reported (the reference is not given) that after injection of 0.05-0.5 mgm. of cobra venom into the arm muscles of a healthy man no change worth noting occurred in these pressures but that in the sick man there was an initial rise and a prolonged fall, less marked in the spinal fluid than in the blood.

The author used *Bothrops* venom (*Lachesis jararaca*) of a strength of 0.2 mgm. in one cc. and *Crotalus* venom (*C. terrificus*) of 0.1 mgm. per cc. The pressures were first taken and then the patient rested for a minute till he was quiet again and the pressures had settled to normal. Now 1 cc. of the venom preparation was injected intraglutely and in 5-10 minutes the pressure was again taken. As Koresnos had found, the author observed no change in normal subjects in the c.s.f. pressure. No initial rise in arterial pressure was found to follow the intramuscular injection only a prolonged fall slight rise followed intravenous injection of *Crotalus* or *Bothrops* venom and the subsequent lowering of pressure was less with *L. jararaca* than with *C. terrificus*.

Twenty-six patients were the subjects of the tests, patients suffering from various nervous diseases: general paralysis, schizophrenia, imbecility, manic depressive psychosis etc. and the results of the pressures before and after the injections are given in a table. In the majority the blood-pressure was still low half an-hour after the injection more marked with the *Crotalus* venom. As regards the cerebrospinal fluid pressure a fall of less than 4 mm. was present in three cases, of between 4 and 8 mm. in fifteen, and of more than 8 mm. in three cases.

H. Harold Scott

DERMATOLOGY AND FUNGUS DISEASES

MARSDORFF, A. Beziehungen der Klimatologie und Ethnologie zur Entstehung von Hautkrankheiten in Anatolien [The Relation of Climate and Race to Skin Diseases in Anatolia.] *Schweiz med Woch* 1944 Aug 5 v 74 No 31 842-8 9 figs.

The author started to practise in Ankara four years ago after 16 years in a Skin Clinic in Germany. In the first few months he observed many cases of certain conditions which were new to him, except for mere textbook knowledge and he came to the conclusion that apart from the usual causes operating elsewhere others of a climatic or ethnic nature must be taking a share.

Among such diseases the author mentions *chiliditis acnaria* (of which he gives a photograph). This is an inflammation of the lower lip and he saw a relatively large number of cases, some in an acute form, others more chronic with patches of leukoplakia. Sufferers rarely applied to the clinic for treatment. The disease was seen in the spring, but got much worse in the summer, was rare in the autumn and never seen in winter. Those attacked were mostly engaged in open-air employment—builders, peasants, coach-drivers, street workers for example. The condition started as small inflammatory swellings, later becoming vesicles then eroding and crusting over. They were associated with a good deal of pain which made speaking and eating difficult. It was common for relapse to occur in successive summers. In the four years work at the clinic at Ankara the author has seen 184 of these cases. He next enlarges on the temperature and humidity curves in Ankara and the district and demonstrates by charts the relations between these factors and the prevalence of the disease (but now here mentions the most probable explanation, that it is a pellagroid condition).

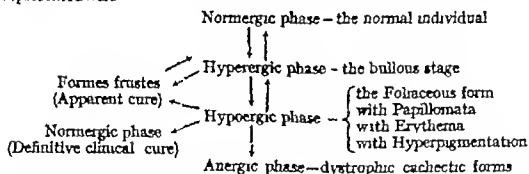
The author next speaks of *prodomia* which in Ankara accounted for 32 per cent of the applicants at the clinic. In Jerusalem this is given as 34 per cent., as compared with 2-5 per cent in other European countries. The Turks are

very cleanly and wash often. The disease is commonest in the summer with high temperature and U V rays abundant and powerful. The author ascribes as causative factors the prevalence of *Phlebotomus* the dust nuisance the reduction of the acid and diastase content of the skin (due to the high temperature and the U V rays) and the transfer of pyococci from the fingers to the skin of the face and the improved conditions for growth of bacteria there on account of the heat.

A notes added in conclusion on the rarity of certain other diseases especially those affecting the genitalia he mentions in particular balanitis herpes carcinoma of the penis gangrenous or phagedaenic ulcer associated with Vincent's spirillum and *Fusiformis fusiformis* H Harold Scott

TORRES U L. Conceito clinico do penfigo foliáceo brasileiro [Clinical Concept of the Brazilian Form of Pemphigus Foliaceus.] *Arquivos de Dermat e Sifiligráfia de São Paulo* 1944 June v 8 No 2 86-125 35 figs [25 refs.]

Pemphigus foliaceus the *fogo selvagem* or wild fire of Brazil may be a truly terrible disease [see this *Bulletin* 1927 v 24 451 1943 v 40 487 488]. The author maintains that the disease is not the same as the *Pemphigus foliaceus* of Europe the differences are important. In the first place in Brazil it has two stages an acute bullous or erythematobullous stage and a chronic exfoliative stage again European cases rarely recover in Brazil 10 per cent (some say 15-20 per cent) undergo spontaneous cure and abortive *formes frustes* occur and it is seen in certain foci. The European disease is one of adults in Brazil it is more common in adolescents and young adults and finally in Brazil the mucosae are never involved as they may be in the European form (though not often). The author's scheme of the development and phases of the disease is as represented here —



The author suggests experimental work on the lines of injecting specific cytolyzins prepared from animal skin based on the analogy of blood-sucking insects causing minute lesions and leading to the formation of cytolyzins and the action of streptococci which are invariably present in the lesions of this disease and play their part in keeping up the condition. Notes are given of thirteen cases with copious photographs depicting the disease in its different stages. H Harold Scott

STARLING P. Sobre a etiologia allergica do penfigo (fogo selvagem). Nota prévia. [Allergy as the Cause of Pemphigus (Wild Fire)] *Brasil Medico* 1944 Aug 5-12 v 58 Nos 32 & 33 295-8.

The author calls attention to factors common to pemphigus and other allergic conditions as evidence that the first is also allergic, First heredity the frequency with which one or other parent is allergic second the disease is chronic like asthma epilepsy and eczema third the presence of eosinophilia fourth

the records of spontaneous cure fifth the likelihood of relapse sixth its non-contagiousness and absence of fever He states that it attacks chiefly the poorer classes because they more than others live almost entirely on one sort of food—meat, beans, rice flour coffee—and those living in certain parts of the country because in those parts certain foodstuffs are grown almost exclusively Among his patients were those allergic to coffee, milk, Guinea-grass (pó de capim) orange French beans and manioc. He concludes by relating two cases cured one by a miracle, the other by spiritism as he calls them [by penance and by pique would be equally true]. The first was a man who had suffered from the disease for 15 years. He was a great meat-eater and as a penitential act vowed to abstain from meat for the future his pemphigus cleared up. The second lived almost entirely on milk from his own cows. These failed and the city authorities introduced pasteurization and forbade the selling of non-pasteurized milk. In disgust, and saying that pasteurized milk upset his liver he ceased to drink milk and his pemphigus began to clear up from that time. He had suffered from the disease for 20 years prior to this and he has now been free from symptoms for two years. (Not a very satisfying paper!)

H Harold Scott

HATCH W E. & WELLS A H Actinomycosis of the Urinary Bladder complicating a Case of Madura Foot. *J Urology* 1944 Aug v 52, No. 2, 149-52, 1 fig [11 refs.]

After a compound fracture of the lower third of the right leg in a man aged 42, a condition of mycetoma developed. The disease behaved to be tuberculous remained localized in the affected part giving rise to much swelling and distortion of the foot with smears discharging thick pus. Ten years after the onset of the mycetoma the man suffered a series of attacks of haematuria each lasting two to three days. Two years later the haematuria became very severe and continuous and the patient was admitted to hospital suffering from the effects of haemorrhage from which he died 24 hours later.

At autopsy actinomycosis of the posterior wall of the bladder was discovered, and the foot lesion was found to be of a similar nature. Culture of the fungus was not obtained.

The case is of particular interest because actinomycosis of the bladder is uncommon and metastatic spread of the disease from a mycetoma is extremely rare.

J T DUNCAN

FISCHMAN J Systemic Blastomycosis with a New Form of Therapy *U.S. Nat. Med. Bull.* 1944 Oct v 43 No. 4 758-61 3 figs.

A woman aged 19 was found to be suffering from blastomycosis (Gilchrist's disease) proved by isolation of the causative fungus *Blastomyces dermatitidis* with involvement of the lungs, the bones of the tarsus and the skin. Surgical treatment, subsequent administration of sulphanilamide and sulphathiazole regulated by daily determination of the drug concentration in the blood, for a month, and then intensive treatment with iodides by both oral and intravenous routes, and local treatment of the lesions with phenylmercuric nitrate, chemical coagulants and ultraviolet rays were all without apparent good effect. [Presumably vaccine treatment was not tried.] At this stage a new treatment was introduced, which consisted of the local application of ether to the skin and bone lesions, and internal administration by giving 4 oz. of ether in 4 oz. of oil by the rectum once daily on nine consecutive days. There was an early and marked improvement both in the local lesions and the general symptoms and an X-ray examination showed a partial clearing of the lung shadows. The daily

ether administration by the rectum was resumed for a further seven days and then once weekly up to the end of three months when the patient was discharged from hospital apparently cured. Confirmation of cure was obtained three years later when the patient died from the effect of an overdose of barbitone and no evidence of the previous blastomycosis was found at the autopsy.

J T Duncan

LEE R. V. Coccidioidomycosis in Western Flying Training Command California & Western Med 1944 Sept v 61 133 (Summary taken from J Amer Med Ass 1944 Dec 2 v 126 No 14 918-9)

Lee says that all new personnel coming to the airfields are skin tested and the negative reactors are retested six months later. All suspicious clinical cases in the dispensaries and hospitals are skin tested and in addition specimens of blood are sent to the Army Epidemiological Board for confirmatory evidence when indicated. Over a quarter of a million skin tests have been given a thousand or more clinical cases recognized and nine complete necropsies done. The author differentiates three forms of coccidioidomycosis: primary, intermediate and advanced. The primary form is usually subclinical. The only evidence of its having occurred is the finding of a positive skin test in an individual who was previously negative. This will occur in about 10 per cent of personnel but some stations have reported as high as 80 per cent of the post population turning positive. Frequently what would ordinarily pass as a cold, mild influenza or 'desert rheumatism' is properly diagnosed as coccidioidal infection. When erythema nodosum occurs the diagnosis is suspected much more frequently. The intermediate (or pulmonic) stage is the one which is most frequently recognized clinically. This is an acute, subacute or chronic pulmonary inflammation. It resembles tuberculosis. Cavities occur frequently but they show a great tendency toward spontaneous closure. The advanced or disseminated form is about 100 times as likely to occur in the Negro as in the white soldier. Dissemination if it occurs is likely to occur early. If there are going to be late disseminations the problem will be very difficult. In the disseminated cases almost every organ of the body has been involved: the body may be literally riddled with cold abscesses. There have been a few cases of dissemination in which apparent recovery occurred. That dissemination may be impending can often be anticipated from a rising titer in the complement fixation test. There is no effective treatment.

HEAT STROKE AND ALLIED CONDITIONS

ALLEN S. D. & O'BRIEN J. P. Tropical Anhidrotic Asthenia: a Preliminary Report. Med J Australia 1944 Sept. 23 v 2 No 13 335-6 1 fig

In the textbooks on tropical diseases a type of heat exhaustion is described in which there is said to be loss of diminution of sweating but in general few details are given. This paper will therefore be quoted at some length as it contains much that is new.

The description is based on 22 cases seen in Northern Australia and New Guinea. The patients nearly always gave a history of prickly heat which had been extensive and severe in most cases however it had disappeared three or four weeks before the loss of sweating began. Symptoms began insidiously and were first noticed in the heat of the day: exercise produced an unusual degree

of exhaustion together with dyspnoea, palpitation, headache and giddiness. Some patients complained of a hot tight prickly feeling in the skin and some at this stage noticed that they were sweating less than usual. At first the symptoms passed off with rest in a cool place but once established, they tended to recur more and more easily and with greater severity until exhaustion supervened. In an attack, the patients were distressed and apprehensive, the pulse rate rose to 100 per minute, the temperature (100-102°F. by mouth) rose and the face became red and face sweat

[illegible]

The arms and fingers and less often the legs were no longer vesicles but deeper than those of the trunk. The amount of obliteration of the natural creases but there was no obliteration of the axillary and inguinal lymph-glands were normal. The most cases the axillary and inguinal lymph-glands were normal though no figures are and tender.

No changes were found in the nervous system or blood-pressure and composition of the urine were it is said, normal though no sugar was given.

With rest in a cool atmosphere the pulse-rate responded rapidly to normal. Full sweating was re-established more or less completely within 14 days. The only outward signs of the disease seen were impetigo of the face. In spite of the reduction in sweating, no case progressed to hyperpyrexia. No special treatment was adopted apart from rest in a cool ward, and graded exercise in the cooler part of the day.

The histopathology of the skin was studied in serial sections of biopsy tissues. The changes are rightly described as of unusual interest. They occurred almost exclusively in relation to the sweat-glands and their ducts, and may be summarized as follows:—

Conclusion of the mouth of the sweat ducts is exclusively in relation to the Malpighian layer by cystic dilatation, as follows:—

- (1) Occlusion of the mouth of the sweat-duct by a minute plug of keratin and nucleated crescent-shaped cells
 - (2) Formation of a small vesicle in the Malpighian layer by cystic distension of the occluded duct which sometimes ruptured
 - (3) Lymphocytic infiltration and dilatation of lymphatics round the duct immediately below the vesicle in the papillary layer of the dermis
 - (4) Dilatation of the whole lumen of the dermal part of the duct to two or three times its natural size.
 - (5) Moderate distension of the sweat-gland acini, with some degree of distortion and atrophy of the secreting cells.
 - (6) Accumulation of tissue fluid in the tissue spaces of the dermis, and dilatation of the lymphatics especially round the sweat glands and their ducts.
 - (7) A slight degree only of vascular congestion.
 - (8) Blockage of hair follicles by a layer of keratin, resulting in distension of follicles with sebum and atrophy of the hairs
- It is considered that the basic cause of the histological changes is the hyperkeratosis which occludes the ducts. Sweat is still formed but cannot reach the

(5) Accumulation of lymphatics especially in the dermis.

(7) A slight degree only of vacuolation of the epidermis.

(8) Blockage of hair follicles by a layer of keratin.

(9) Atrophy of the hairs.

(10) The basic cause of the histological changes is still unknown.

(7) A slight degree only of vascular congestion
(8) Blockage of hair follicles by a layer of keratin, resulting of follicles with sebum and atrophy of the hairs

It is considered that the basic cause of the histological changes is the hyperkeratosis which occludes the ducts. Sweat is still formed but cannot reach the

skin surface after bursting out of the ducts it is reabsorbed by the lymphatics and carried to the regional glands which become enlarged. The general symptoms may result simply from the reduction in evaporative cooling in a climate where this is essential for the regulation of body temperature. On the other hand the authors believe that part of the symptomatology is referable to the abnormal internal circulation of the sweat.

[In the past year (1944) in addition to this paper two other descriptions have been published of heat exhaustion accompanied by reduction in sweating (WOLKIN GOODMAN & KELLEY this *Bulletin* 1944 v 41 785 LADELL WATERLOW & HUDSON *ibid* 1945 v 42 143). This syndrome differs in almost every way from the classical type of heat exhaustion or prostration. Since it has not hitherto been clearly defined as an entity it may be of interest to contrast the findings of the three groups of workers. In general they agree very closely and this is noteworthy since the work was done in regions as far apart as Northern Australia and New Guinea the American desert and the desert of Southern Iraq.

In N Australia the humidity is fairly high (70-80 per cent relative humidity with a dry bulb of 80-85 F (*Commonwealth Bureau of Meteorology Melbourne Bull No 14* 1916) during the months when the cases occurred. In the desert regions the humidity is very low—about 30 per cent—and the dry bulb temperature reaches 120°F.

The symptomatology described by Ladell Waterlow and Hudson in Iraq is almost identical with that recorded by Allen and O'Brien. Both groups of authors mention prickly heat as an antecedent both say that the prickly heat usually cleared up or improved before the onset of symptoms. In the reviewer's patients the onset of symptoms coincided with the disappearance of acute prickly heat whereas in Allen's there was an interval of 2-3 weeks. Wolkin *et al* make no mention of prickly heat but say that loss of sweating was often preceded by a period of distinct outpouring of sweat lasting several days or weeks. In the Iraq cases as in Allen's the symptoms were brought on by exertion particularly in the heat of the day.

All three clinical accounts agree on three important points (a) that the body temperature was only slightly or moderately raised in contrast to hyperpyrexia (b) that the skin was dry and sweating appeared to be diminished over part or all of the trunk and limbs and (c) that sweating was always profuse on the forehead and face. In hyperpyrexia these parts are dry like the rest of the body.

There is some disagreement in the descriptions of the skin. Wolkin *et al* like Allen and O'Brien say that it had the appearance of gooseflesh. They add that in cases of longer standing there was a fine branny desquamation. Allen and O'Brien also found desquamation and ichthyosis especially of the legs in a few cases. In the reviewer's patients in Iraq the appearance described as gooseflesh was not seen the typical finding was desquamation which was present to a varying degree in almost all cases. It was most severe on the legs which were sometimes ichthyotic. Thus although there are important differences there are also certain common features in the three accounts.

All the authors agree that the general symptoms responded rapidly to rest in a cool place but that normal sweating and a normal condition of the skin are restored more slowly. Impetigo and skin sepsis as a complication are mentioned by both Ladell *et al* and by Allen and O'Brien. Both these groups point out that the diagnosis may easily be made of a functional nervous disorder unless the condition of the skin is taken into account.

Wolkin *et al* produced objective evidence of reduction in sweating by comparing the sweat response to heat and to pilocarpine on admission and on recovery. Starch iodine powder was used as an indicator. Ladell *et al* showed that patients of this type had an abnormally high skin temperature and were

[April 1945]

unable, under some conditions, to maintain a constant body temperature. The American authors could not decide whether the failure of the sweating-response was due to a central or peripheral cause. Ladell *et al* inclined to the view that the cause was peripheral but unlike Allen and O'Brien they found no pathological changes in the sweat-glands. They did not however examine serial sections.

The syndrome described in Iraq contains one prominent feature which is not mentioned in either of the other accounts—polyuria. In some cases this amounted to 10 litres a day. It began at the time of onset of the other symptoms and often persisted for days or even weeks after admission to hospital. A thorough chemical investigation of these cases was carried out. The only abnormality was a slight diminution in the chloride content of the plasma (about 90 milli Equiv. per litre) with a normal output of chloride in the urine. (In classical heat exhaustion the urine contains no chloride.) In Wolkien's series laboratory investigations were made in a few cases but no reduction of plasma chloride was found. Wolkien and Ladell agree that salt had no beneficial therapeutic effect.

It will be seen that many points in this syndrome are still obscure. The practical importance of understanding and preventing this disease is emphasized by Ladell *et al*. In their quateral (soldiers in the desert) it was by far the commonest disability produced by heat, and, though not severe or dangerous, caused very great loss of time and efficiency.] Waterloo

ELEKTOV J. R. & WINKLER A. W. *Physiologic Effects of Drinking Undiluted Sea Water* War Medicine Chicago 1944 Oct. v 6 No. 4 241-6 4 charts [Refs in footnotes]

The emphasis in this paper is on the physiological dilemma presented to the body when a man drinks hypertonic saline with a higher chloride concentration than can be excreted in the urine. Two things may happen: either the excess salt is excreted at the expense of body water or it is retained. The retention will involve a redistribution of body water: the extracellular fluid increasing at the expense of the intracellular. In a critical review of other authors' work on thirsting men, Elkinton and Winkler show that in all experiments there was a loss of body water and a hypertonicity of the body fluids when sea water was administered. These experiments on human subjects were all necessarily on the comparatively early stages of the condition. But the present authors, using dogs instead of men, have been able to follow the changes until death. As dogs can excrete up to 3.5 per cent NaCl in their urine, to produce the analogous experimental situation. 5 per cent saline was administered.

When the strong saline was given to dogs in water balance the toxicity of the body fluids rose and there was a shift of water from the intracellular to the extracellular phase. When given to animals previously deprived of water for some time, some of the extra salt was retained, and as a result the analogous water but an increasing proportion was retained. The same shift of water into the extracellular phase occurred, and as a result the circulation while the intracellular volume progressively diminished.

Death in these animals was not from circulatory but from respiratory failure preceded by disturbances in the central nervous system. The authors consider that the few clinical descriptions in man of death after drinking sea water correspond to the picture seen in their dogs. They interpret the nervous changes as being due to the cells of the central nervous system participating in the general cellular dehydration.

In their discussion they point out that the urinary volume during dehydration is largely determined by the urea to be excreted hence it is not a good thing for thirsting castaways to subsist on fish [The diuretic effect of protein and extractive during dehydration was taken into account in preparing M.R.C. War Memorandum No 8 (*Bulletin of War Medicine* 1943 Apr v 3 No 8 463) this had been shown by experiment and as a result it was advised that meat pemmican should no longer be issued in the emergency ration. The obligatory urine volume of 400 cc per day taken as a basis for certain suggestions by British workers referred to men on the low protein diet recommended by the M.R.C. with the pemmican diet higher volumes were found As Elkinton and Winkler point out on a completely nitrogen free diet very low urine volumes may occur]

W S S Ladell

RIEMERSCHMID Gertrud. Some Effects of Solar Radiation and other Factors of Climatic Environment on Human Beings. *South African Med J* 1944 Nov 11 v 18 No 21 365-8.

Various scales of warmth which take into account other thermal factors besides air temperature are discussed. Some observations made in Johannesburg Durban Nairobi and on the Island of Föhr North Sea with the 'cooling ball' or frigograph of Pfeleiderer are recorded. This instrument takes into account air temperature air velocity and radiation but ignores humidity [The records would have been of more value if there had also been given some information about air temperature and wind speed]

Maximum and minimum temperatures at Davos Belfast (S.A.) Kew and Durban (S.A.) are also tabulated

The main theme of the paper is that one or other of these special scales of warmth should be used when the physiological effects of meteorological conditions are being studied.

T Bedford

i JOEL, E. Physiological Data showing that Standards of Physical Efficiency and of Heat Resistance of African Natives are High *Clin Proc Cape Town*. 1944 Sept. v 3 No 7 355-6 361-76 8 figs. [17 refs]

ii — Body-Weight as Determinator of Physical Efficiency [Correspondence] *Nature* 1944 Dec 30 830 1 chart

1 In experiments made by American workers negroes performed standard work tests with heart rates several beats below those of white subjects and the conclusion is drawn that this difference indicates a greater efficiency of energy transformation or of cardiovascular function on the part of the negroes. In maximal work tests the negroes attained higher maximal heart rates. Judged by the oxygen consumption during work the whites were less efficient than the negroes allowance being made for body weight. The American investigators concluded that the trained negro of relatively pure racial stock is more skilful in walking and climbing than the white man and that the negroes were able to use their oxygen debt to a greater extent.

Further studies carried out in humid heat showed that black subjects were superior to whites in various essential physiological adjustments. The negroes kept cooler than the whites mainly because they produced less heat. Negro sharecroppers maintained lower body temperatures than any of the other groups studied.

Statistical evaluation of the results of physical efficiency tests conducted as part of the National Manpower Survey for South Africa indicates that among comparable groups of Hantu Chinese Cape Coloured European and Indian

school children, Bantu children show on the whole the highest performances in running 100 yards (speed test) and 600 yards (endurance test).

In the Olympic Games members of the African races have scored several times as many successes as would be expected on the basis of their share of the world population. The Watutsi tribe of Ruanda-Urundi in Central Africa produce outstanding high jumpers. Hundreds of Watutsi young men jump over 6 ft. and often 8 ft 2 in. Record jumps of 7 ft 2 in. are reported.

ii. The letter to *Nelsons* summarizes the results of a study of the effects of the body weight of S. African schoolboys on their efficiency in three tests of physical fitness viz (i) running 100 yards which tests circulatory and muscular skill and speed (ii) running 600 yards which tests muscular and respiratory endurance and (iii) putting the 12 lb shot—a test of muscular strength. The 1514 boys of between 6 and 17 years of age were divided into four groups according as they were underweight or overweight on the basis of aldwin and Wood's age-weight tables. The boys in group A were underweight 7 per cent or more below normal group B were slightly underweight, but more than 7 per cent below normal group C included the normal boys and those whose weight was less than 15 per cent above the normal.

In both the 100 yards and the 600 yards the extreme groups A and D that is the distinctly underweight and overweight groups, both put up performances that were significantly poorer than those of the intermediate groups. The performances of the intermediate groups did not differ significantly from each other in either test. In the 100 yards the poorer performances of the extreme groups did not differ significantly from each other but in the 600 yards the fat boys of group D made a distinctly poorer showing than their fellows in group A.

In putting the shot the average performance increased progressively from group A to group D but the differences between groups B and C and between groups C and D were not statistically significant. The one clear point here is that the underweight boys of group A put up a poorer performance than any of the other three groups.

T. Bedford

MISCELLANEOUS DISEASES

URNBULL H. H. Tropical Diseases in Returned Soldiers. *Med J Australia* 1944 Oct 14 v 2 No 16 397-401

The author points out the difficulties which civilian medical officers in Australia may encounter in diagnosing and treating various tropical diseases in returning troops owing to their unfamiliarity with these diseases. The most important of these diseases are malaria, dysentery and scrub typhus.

Malaria—The present routine course of treatment [details not given] allowed by 0.1 grammes of Atebrin (mepacrine) per day for six weeks will produce cure of malignant tertian malaria in almost 100 per cent. of cases. This does not apply to benign tertian malaria but the course of mepacrine will postpone relapse. Every soldier who lands in Australia from New Guinea or other Pacific Islands is given a six-week supply of the drug and medical men should contradict the statements that it may cause sterility or damage the liver. Another point to remember is that malaria may give positive results in serum tests for syphilis.

Dysentery.—In New Guinea sulphaguanidine produced magical effects in bacillary dysentery. Amoebic dysentery is much less common in New Guinea than in the Middle East; it exists also in Australia. The diagnosis and treatment are discussed and complications (hepatitis and liver abscess) are referred to.

Scrub typhus.—This was common among the troops in New Guinea and caused a number of deaths. It does not cause permanent damage to the heart and patients usually recover in 4–6 weeks, occasionally after more than 4 months.

Schistosomiasis and *ankylostomiasis*.—The former is uncommon, the latter common in New Guinea. A single dose of 4 cc. of tetrachlorethylene together with 1 cc. of oil of chenopodium is recommended for ankylostomiasis. If necessary it may be repeated after ten days.

J. F. Corson

FAUST E. C. Diseases in the Tropical War Zones. V The Diseases of the Far East, Southwest and South Pacific. *Gastroenterology* 1944 Sept. v. 3 No. 3 163–87 10 figs [figs. 32–41] [50 refs.]

In the fifth part of this series of papers the author treats the subject in the same way as in the earlier papers. In the section on malaria a useful list is given of the chief vectors with their distribution and breeding places. The other diseases specially to be noted include amoebiasis hookworm infection (in clodging foci of *A. brasiliense* in Malaya and the Philippines) clonorchiasis filariasis scrub typhus and plague.

[For earlier papers in this series see this *Bulletin* 1944 v. 41 966–967 1945 v. 42 154.]

Charles H. Hocks

SOARES T. Acerca dalguns problemas de assistência relativos aos trabalhadores indígenas de África [Health Problems regarding African Labourers.] *África Médica* Lisbon 1944 Aug–Sept. v. 10 Nos 8–9 165–80 3 charts

The problems considered and the advice given in this contribution are such as are to be found in all works on tropical hygiene, but the article is useful as indicating the diseases prevailing in the Angola district.

Workmen before being engaged should undergo a physical examination and only those reaching a certain standard should be recruited. Those accepted should be placed in camps under conditions as like as possible to those amid which they are going to work for preparation and acclimatization and they should be vaccinated against smallpox, enteric fevers, diphtheria and meningitis [but see later], be rid of intestinal and ectoparasites and treated for any ailments from which they are suffering—malaria, yaws, trypanosomiasis [it seems hardly likely that a sufferer from trypanosomiasis would be accepted as a labour recruit]. If means of transport are not available the men should not march on foot, stages greater than 20–25 kilometres a day. Notes on housing, water-supply and food follow. In the Belgian Congo each labourer is given 500 gm. of meat, 600 gm. of manioc flour, 70 gm. of palm oil, 150 gm. of legumes and fresh fruit and 15 gm. of salt or about 3,400 calories daily. They also eat fish and groundnuts making up another 600 or so calories.

As regards provision for treatment of disease it is suggested that hospital beds should be at the rate of 5 per cent. of the workers and any hospital of 100 beds should have a dispensary for outpatients, place for small operations and a pharmacy, rooms for 3–4 beds each and a small maternity section, wards for isolation, rooms for disinfection, for baths, store for clothes, room for laundry and ironing, a kitchen, refectory and a mortuary.

The diseases chiefly met with are malaria, amoebic dysentery, ankylostomiasis, pneumonia (often very acute ending fatally within 48 hours), yaws, venereal diseases, especially gonorrhoea, relapsing fever carried by *Ornithodoros moubata* and sleeping sickness for which trypanamide is used exclusively, in

with technique a word or two on the subject of culture which is of some diagnostic value might not have been out of place. The intestinal flagellates are carefully described and it is interesting to note that the name *Retortamonas* is used for the name *Embadamonas*.

Chapter 7 is devoted to the trypanosomes and leishmania. As regards the former the illustrations of *Trypanosoma gambiense* and *T. rhodesense* leave much to be desired and they fail to depict the characteristic polymorphism of these organisms. The account of the leishmania is accurate but more definite reference to the work on the transmission of oriental sore and kala azar by sand flies should have been made. In Chapter 8 the malarial parasites are dealt with and in Chapter 9 the technique for the detection of protozoa of the circulatory system. Chapter 10 is devoted to a consideration of objects which may be confused with blood-inhabiting protozoa but one would hardly have included in this category as the author does the normal white blood corpuscles. In the final chapter descriptions and illustrations of *Sarcocystis lindemanni* and *Trichomonas vaginalis* are to be found.

The author's method of writing the scientific names does not conform to the rule thus he gives *Trichomonas vaginalis* Donne 1837 without a comma between the Donne and the date. This omission occurs all through the book. In some places the English wording is peculiar there being a tendency to the dropping of the article where it would be expected. In other places it is quite ungrammatical. However these are small points which do not detract from the excellence of the book, which is remarkable for the high standard of its printing paper and binding alike. It is undoubtedly an artistic production and it seems a pity that those who produced the book did not read it more carefully before passing it.

The book, as already noted will be useful to those who are taking up the study for the first time and want no more than a bare outline of the subject.

C. V. HENSON

TROPICAL DISEASES

BULLETIN

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[No 5

SUMMARY OF RECENT ABSTRACTS *

IV TRYPANOSOMIASIS

AFRICAN TRYPANOSOMIASIS

Epidemiology Transmission

MACGOWAN (p 106) reports that in one district on the north bank of the river Gambia the incidence of human trypanosomiasis has fallen greatly in recent years as a result of treatment carried out at a dispensary. On the south side the people are reluctant to receive treatment and the infection rate remains as high as before.

DIAZ VARELA (p 547) gives an account of human trypanosomiasis in Fernando Po where the campaign against this *Trypanosoma gambiense* infection was begun in 1928. The disease still persists.

NASH (p 653) notes that some West African streams are choked by the palm *Raphia* which provides very suitable conditions for *Glossina tachinoides* and which is much used for roofing. The cutting of the poles is therefore a danger in that it entails close contact with the fly. Nash states that a law has been made prohibiting the cutting of the poles except during the first fortnight of each 3-month period. If this is obeyed it will mean that a whole generation of flies (and their infection) will die out between two successive cutting periods.

NASH (p 653) shows that when streams in West Africa become dry the remaining *G. palpalis* tend to concentrate round the water holes dug in the dry river beds. These are much frequented by the people and the danger of infection is evident. A few flies may infect many persons in such circumstances.

CHORLEY (p 463) reports a heavy concentration of *G. morsitans* in Portuguese territory near the border of S. Rhodesia and the presence of *G. pallidipes* in the Wankie district. Animal trypanosomiasis appears to be increasing and human cases are reported for the first time in one area.

VANDERPLANK (p 1010) has compared the attractiveness of certain animals for *G. pallidipes*. Dog, ox and porcupine were the most attractive, next domestic pig (and screens), next sheep, goat, man and baboon, last serval, cat, lion and jackal. The screens, unscented or scented by bush pig, were used for comparison.

VAN EMDEN (p 829) describes a new subspecies of *G. nigrofusca* which he names *G. nigrofusca hopkinsi*. It is found in Western Uganda.

*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1944 v 41. References to the abstracts are given under the names of the authors quoted and the page on which the abstracts are printed.

Aetiology

LAVIE (p. 368) discusses at length the classification of the trypanosomes and the evolution of their morphology. The argument cannot be more briefly stated than in the original abstract which readers are advised to consult. He holds that all the pathogenic forms have originated from trypanosomes of ungulates which originally adapted to the posterior station of their vectors later when they began to be transmitted by tsetse adapted themselves to the anterior station and development in a salivary medium. But adaptation to the anterior station is poor in comparison with the good adaptation to the posterior station of their vectors shown by the non-pathogenic mammalian trypanosomes. This is approximately 100 per cent. whereas infectivity of *T. vivax* for tsetse is about 50 per cent. of *T. congolense* is less and of the *T. brucei* group is very much less.

VANDERPLANK (p. 829) has published a preliminary note of an investigation into the structure of the nucleus of trypanosomes.

PACKCHAWIAN (p. 107) gives the results of a number of experiments on the viability of various trypanosomes and leishmanias in culture details should be sought in the original abstract.

WERNER (p. 653) has cultivated *T. gambiense* in a modification of the leptospira medium used by Noguchi and Battistini incubated at 26°-28°C. In this medium the trypanosomes have been maintained alive for 71 days or by numerous transplants, for 127 days.

It is known that repeated exposure of trypanosomes to sub-effective doses of acidine compounds leads to resistance to acriflavine and to arsenical compounds. LOURIE and COLLIER (p. 370) however have shown that exposure of *T. rhodesense* to mepacrine does not lead to resistance to that compound or to arsenicals and conclude therefore that suppressive mepacrine for the control of malaria can safely be given to men exposed to infection with trypanosomes without risk of development of resistant forms.

Clinical Findings Treatment.

LYNARD (p. 14) has examined daily the blood of patients with (presumably) *T. gambiense* infections and concludes that there is no evidence of cyclical appearance of the trypanosomes. Sleeping sickness may be missed if only one blood examination is made as in routine surveys. His results indicate that examination of sternal puncture material is a more certain method of diagnosis than blood examination.

CHOUKARA (p. 14) has found trypanosomes in the ascitic fluid of a child in West Africa.

SCOTT (p. 733) has investigated the eyes of a series of patients with *T. gambiense* infection. Keratitis was common but was usually due to trachoma only in 1 of 42 cases could it be attributed to trypanosomiasis. Irido-cyclitis was found in 7 of 150 cases. Scott advises the testing of vision before each injection of trypanamide because of the danger of arsenical optic atrophy. The slightest diminution of visual acuity is an urgent sign that treatment must be stopped.

FULTON and YORKE (p. 15) have examined the therapeutic efficiency of six drugs in trypanosome infections of mice. The paper cannot usefully be condensed and should be consulted in the original. The drugs included trypanamide, novarsenobion diamidines and a phenanthridinium compound. Differences in efficiency are noted according to the route of administration employed.

MURAZ (p. 734) reports not unfavourably on the value of three arsenical preparations in West African sleeping sickness.

POTTER (p. 370) gives an account of four cases of acute visual impairment after the administration of trypanarsamide: this condition has received less attention than chronic affections. In all there was contraction of the visual field which improved somewhat within a few weeks. The author thinks that this type of accident is probably a result of idiosyncrasy. No contra-indication to trypanarsamide had been found at ophthalmoscopic examination before treatment was started though such examination can guard against progressive deterioration of vision due to the chronic type of trypanarsamide reaction. Injections of thiamin and spinal drainage have little therapeutic value in these cases.

SANDGROUND and HAMILTON (p. 372) have shown that in rats *p*-aminobenzoic acid has great power to detoxify certain pentavalent arsenicals (including trypanarsamide) without interfering with their trypanocidal action against *T. equiperdum*. This effect was present if the PAB was given (orally or by injection) at the same time as or shortly before the arsenical when given after the arsenical however PAB showed great reduction of protective power. PAB alone is not trypanocidal.

BOMFORD (p. 1008) reports a case probably of *T. gambiense* infection in a European from Sierra Leone. Treatment with pentamidine was successful in producing clinical cure and in reducing the cerebrospinal fluid cell count to 4 per cmm, and the protein to 0.03 per cent.

HARDING (p. 1009) in discussing the paper by Bomford (above) reviews his own experience with pentamidine and the more well known drugs in 2,000 cases in West Africa. In early cases pentamidine is about as effective as Bayer 205 followed by trypanarsamide but in late cases is much less effective than these drugs. Pentamidine has little value once the central nervous system is affected: the dividing line is around 10–15 cells per cmm. [In comment CORSON points out that protein content may be a more important guide than cell count.] Pentamidine may be given concurrently with trypanarsamide and this system has produced good results even in late cases. Results cannot be well assessed unless the patient is observed for at least one year.

MCCOMAS and MARTIN (p. 466) report a case of sleeping sickness in a West African soldier who died in status epilepticus after the third injection of pentamidine. Post-mortem examination showed that the infection was of considerable duration.

VAN HOOF, HENRARD and PEEL (p. 928) have investigated the action of pentamidine in the treatment and prevention of *T. gambiense* infection. In treatment their results were not unlike those reported by others—the drug was not satisfactory in late-stage disease. Like Bayer 205 pentamidine apparently has a prolonged action with a slow rate of elimination or excretion. Two volunteers given injections and subsequently exposed every few days to infective bites did not show trypanosomes in the blood for 10–12 months but no controls were used and HAWKING comments that these results permit the alternative explanation that the infecting strains may have been feebly pathogenic for man. A prophylactic experiment in certain villages heavily exposed to infection indicated some protective action during three months of observation after injection of pentamidine.

FULTON (p. 929) has carried out experiments on the prophylactic action of various aromatic diamidines in mice subsequently inoculated with *T. rhodesiense* or *T. congolense*. The prophylactic effect which is proportional to the curative index, lasts about 2–4 weeks and Fulton states that if frequent inoculations of *T. rhodesiense* are made after the drug injections protection is apparent for 8–24 weeks but it is due to immunization by the trypanosomes and not to the drug (after the first 2–4 weeks). He criticizes the work of VAN HOOF *et al.* (above) in this sense.

Control.

The Department of Tsetse Research, Tanganyika Territory (p. 460) has issued a report of its activities since 1938. A 7 year programme of work was begun in 1938 but as a result of the war several schemes have necessarily been closed down. Nevertheless, a great deal has been accomplished. The report deals with studies made of six of the eight species of *Glossina* known to exist in the Territory. JACKSON has found that *G. morsitans* as a rule keeps to a restricted ambit but that there is a slow outward drift of flies which escape and establish themselves in new ambits. *G. swynnertoni* has a greater tendency to disperse concentrating in the hard pan in the rainy season and spreading outwards in the dry weather. Fire exclusion reduces the numbers of *G. swynnertoni* especially if trees and thickets in the hard pan areas are felled but though the remaining flies are few the females are still fertilized to a depth of about 100 feet from the edge of water causes great reduction in the numbers of *G. palpalis fuscipes* though it does not interfere with their food supply and they still breed in the inland thicket. Work has also been done on *G. pallidipes*, *G. brevipalpis* and *G. austeni* by MCGRIDGE and VANDERPLANK and the latter with POTTIS and FORD has engaged in various laboratory investigations. BAX has made experiments on the senses of smell and sight of *G. swynnertoni* and many other investigations details of which must be sought in the original, have been made by the members of this active team of workers.

BAX (p. 463) enunciates a practical policy for tsetse reclamation in East Africa. He notes that in the last 20 years about 1 000 square miles of Tanganyika Territory have been freed from flies, but that in the same period thousands of square miles have become infested. As a result of advances in knowledge made in recent years, the whole conception and emphasis of tsetse reclamation is changing. He considers in turn the measures which could be taken to clear the various types of country—cultivation steps, thorn savannah, miombo wooding, the great plains carrying a lace-work of vegetation. The details of his recommendations cannot effectively be condensed, and should be sought in the original. The prospects for large-scale reclamation are good in certain parts of the country and the author quotes instances in which a relatively small amount of work has opened up large areas or so reduced the fly population that settlement has been possible. This is an important paper which must be taken into account in any scheme of tsetse fly control that may be projected.

FAIRBANKS (p. 12) has reviewed the agricultural problems posed by sleeping sickness settlements in Tanganyika Territory. When inter-tribal war was prevented by European administration the natives left their defensive clearings and tended to live in more scattered small communities in the bush country where contact with tsetse was more intimate. This resulted in loss of cattle and when human trypanosomiasis appeared, in outbreaks of sleeping sickness. The ultimate aim in these clearings is to provide 16 acres of land for each family and the people are urged first to produce food crops and later to keep animals. The problems raised by these measures include preservation of soil fertility and the production of clarified butter, hides and meat for export to provide the means of paying for transport. These questions are discussed, and the author points out that in this way educational, medical and other facilities are brought to the people.

CHORLEY (p. 269) gives an account of tsetse control operations during 1940 and 1941 in S. Rhodesia where near the Portuguese border there has recently been some considerable extension of cattle trypanosomiasis. *G. morsitans* has invaded the area, and in consequence a programme of game destruction has

been undertaken over 15 500 animals were shot in 1940 and 20 500 in 1941. A large scheme of native settlement was planned for 1942 in an area of fertile virgin land which at the time was being rendered safe.

The relative proportions of the first and later stages of West African sleeping sickness among cases diagnosed for the first time are regarded by MURAZ (p 734) as a good indication of the efficiency of the preventive measures in force. Patients with 0-5 cells per cmm cerebrospinal fluid are in the first stage; those with more than 20 are in the second stage; the intervening proportion being regarded as doubtful. If frequent inspections of the population have been made early cases will have been diagnosed and cured; if not these cases will have passed on to the later stages. In the original MURAZ gives details of findings for 1940 in 31 sectors of the seven French colonies; in only four were the prophylactic measures apparently satisfactory. Nevertheless much good work has been done in spite of war time difficulties.

Trypanosomiasis of Animals

FULTON and YORKE (p 373) have tested certain drugs in *T. congolense* infections of mice. Results should be sought in the original but it is noted that the two most active substances were a phenanthridinium compound and diamidino dimethyl stilbene. Bayer 205 was inactive.

CARMICHAEL and BELL (p 373) have treated cattle infected with *T. congolense* with 4,4'-diamidino dimethyl stilbene. Cure was effected in some animals but in doses which gave acute fatal poisoning in others.

FUNK *et al* (p 734) report on the trypanocidal value (on *T. brucei* in mice) of certain derivatives of ethylene diamine. These belong to a group of drugs whose trypanocidal action was not previously known but which show some promise.

TALLAFERRO and OLSEN (p 15) discuss the protective action of normal sheep serum against *T. duttoni* of mice.

HORNBY and FRENCH (p 107) have experimented with repellents for animals exposed to tsetse. A pyrethrum preparation appeared to offer some protection against attack by flies under natural conditions but as far as infection by trypanosomes is concerned the experiment was inconclusive.

AMERICAN TRYPANOSOMIASIS (CHAGAS'S DISEASE)

Epidemiology Transmission

No case of Chagas's disease has yet been reported from the United States though six species of *Triatoma* have been found infected with trypanosomes indistinguishable from *T. cruzi*. PACKCHANIEN (p 270) has been able to infect a man with trypanosomes from *Triatoma kridermanni* (indigenous to Texas). This man showed typical symptoms of Chagas's disease.

DAVIS (p 271) has in similar fashion produced typical *T. cruzi* infection in monkeys by inoculation into the eye of infected faecal material from North American triatomids.

WOOD (p 108) has found infected hogs in Arizona and names two *Triatoma rubida* and *T. longipes* as the chief vectors.

MARTINS *et al* (p 191) in an account of 25 cases of Chagas's disease found in the State of Minas Geraes remark that although no acute case was seen in a survey of one area more than 20 per cent. of the population harboured *T. cruzi*. An account of this survey is to be published later.

MAZZA and ORIBE (p 375) have found a high proportion of positive results in *Triatomidae* taken in the Formosa area of Argentina. They have experimentally infected a colt but do not report natural infection in horses. Man is also infected.

and apart from the finding of *T. cruzi* in man the authors report positive Guerreiro-Machado reactions in a proportion of persons with signs of cardiac disease. Other human cases are reported by MAZZA and JAUREGUI (p. 375) in the same area.

CHAGAS (p. 374) the son of the man who first described American trypanosomiasis gives a list of the vectors of Chagas's disease and of the animal hosts. The latter include dogs cats armadillos squirrel monkeys a weasel-like animal, opossums ant-eaters pigs and bats.

MAZZA and CHACON (p. 108) have found *Parstrongylus geniculatus* infected with *T. cruzi* in Eastern Bolivia, and give the names of other known vectors in the same country.

MAZZA (p. 378) has examined various Triatomidae in Argentina for developing forms of *T. cruzi*. Some were positive but others though large numbers were taken, were negative. For details the original should be consulted.

A high infection rate of *Triatoma infestans* has been found in part of Chile by BARRERA SEPÚLVEDA (p. 549) and a number of human cases were discovered in the same area. Two dogs and a cat were also found to be infected.

ARNOLD and BELL (p. 830) note that *T. rubrofasciata* is found in Hawaii pointing out that as a well-known vector of *T. cruzi* it constitutes a possible health hazard.

MAZZOTTI and LEÓN (p. 192) have succeeded in infecting nymphs of *Triatoma carrioni* with *T. cruzi*.

MAZZOTTI and OSORIO (p. 16) have infected three species of *Ornithodoros* with *T. cruzi*. *O. hermsi* could not be infected in this way.

Actiology

DIOS and SOMMERVILLE (p. 829) describe their findings on the inoculation of large numbers of white mice with *T. cruzi* from infected bugs and from man. Many mice proved refractory but in those which became infected no appreciable difference could be detected between strains from bugs and from man.

SULLIVAN (p. 1011) has shown that *T. cruzi* present in citrated blood from infected guinea-pigs remained viable (and actually multiplied) for 257 days at room temperature. Examination of such blood including cultivation is a satisfactory method of diagnosis in man.

SENEKJIK (p. 548) gives an account of the biochemical reactions cultural characteristics and growth requirements of *T. cruzi*. Details cannot be further abstracted.

TOM (p. 376) describes a modification of the Novy and MacNeal medium for the growth of *T. cruzi*. This cannot be further abstracted. details are given in the abstract.

MEYER (p. 468) has shown that in tissue culture of brain and spinal ganglia of chick embryos *T. cruzi* invades the nerve cells as well as the other cells of the nerve tissue.

DIOS and BONACCI (p. 468) have failed to infect toads with *T. cruzi*.

DENISON (p. 467) has studied *T. cruzi* infection of rats in relation to reticulo-endothelial blockade.

MAZZA *et al.* (p. 16) have prepared a dialysed filtrate of an emulsion of ground *T. cruzi* which they have used as antigen for an allergic skin test in Chagas's disease. Injection of this substance into the skin gives rise to an immediate reaction in sensitive persons. the authors give a detailed account of the pathology of the skin in such reactions.

WOOD (p. 192) notes that in 1941 ICKHAM found *Trypanosoma desertionis* in a bat in California. This trypanosome closely resembles (and may be) *T. cruzi* and Wood advocates a search for the latter in Central California.

Treatment

FULTON (p 377) has found no significant difference between the Bayer preparation 7602 (Ac) which has been used in the treatment of Chagas's disease and the corresponding ICI synthetic product. In mice infected with *T. cruzi* the therapeutic tests were disappointing the drug has no action on *T. congolense* or *T. rhodesiense*.

CARMONA DE LA FUENTE (p 549) has treated a patient with Bayer 7602 (Ac) symptoms cleared up but the Machado reaction remained positive.

Charles Wilcocks

MALARIA

BUXTON P. A. Rough Notes. Anopheles Mosquitoes and Malaria in Arabia. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1944 Dec. v. 38 No 3 205-14 [21 refs.]

This paper contains a summarized collection of the information available on the geographical distribution of malaria in all the Arab Lands in Asia excluding Sinai, Palestine, Transjordan, Syria and Iraq, and on the anopheline fauna and malaria vectors.

The information on distribution, being itself a summary, does not lend itself well to condensation and should be referred to in the original. The area is divided into three. In Western Arabia malaria is of patchy distribution but severe where it occurs: the southern part of the coastal belt, the valleys which run westwards from the mountains of the Hejaz, Asir and the Yemen, and Jeddah, Wadi Liya, Mecca and Taif are noted as malarious; the upper limit would seem to be as high as 6,000 feet. In Southern Arabia Aden itself is relatively free from the disease, such as occurs being probably caused by anophelines which have been blown long distances by wind, but low-lying ground liable to flooding and oases in the plains may be malarious. In the hills malaria occurs up to an altitude of at least 5,000 ft. and is widespread in the Western Aden Protectorate and the Yemen. In Central Arabia, oasis fever, which is frequent, is almost certainly malaria. On the north-east coast detailed information is available for Bahrain and Dhahran, in both of which malaria is common, as it probably is along the whole coast.

The following anophelines have been recorded: *Anopheles constanti*, *A. dithali*, *A. sergenti*, *A. culicifacies* and *A. culicifacies* var. *adenensis*, *A. arabicus*, *A. subpictus*, *A. gambiae*, *A. turkkudi*, *A. cinereus*, *A. multicolor*, *A. stephensi*, *A. theobaldi*, *A. pulcherrimus* and *A. pretoriensis*. Of these *A. subpictus* and *A. theobaldi* are probably errors. There are also doubtful records of *A. macmahoni* and *A. ruficulus*.

Malaria vectors are *A. gambiae*, *A. culicifacies*, *A. stephensi* and possibly also *A. sergenti* and *A. multicolor*.
G. Macdonald

POYR R. Orographie et paludisme, ethnographie et habitation, dans le nord de l'Indo-Chine. [Orography and Malaria, Ethnography and Housing in the North of Indochina.] *Bull. Soc. Path. Exot.* 1943 May 12 & June 9 v. 36 Nos 5-6 167-73 17 figs on 6 pls.

This lucid though condensed description of the northern third of French Indo-China is the outcome of a 28 months' stay in that country during which the author made expeditions aggregating 4,000 kilometres. The area described comprises the whole of Tonking and the northern ends of Annam and Laos.

down to 17". One-tenth of this large area is composed of the alluvial Red River Delta. The rest is hilly or mountainous, the ranges running mostly from the north-west to the south-east. The delta, apart from a few wooded outcrops is practically free from malaria. In the middle region there is but little endemic malaria in the open plains but in the wooded portions the endemicity is considerable. In the high region very high malaria endemicity prevails but its intensity is rather a function of orographic conditions [physical conditions of mountainous areas] than of altitude or latitude. In general the valleys are heavily impregnated with malaria up to a height of 1,200 metres the narrower the valley, the more shut in and wooded it is, the higher the endemicity, but the open valleys are by no means immune from attacks of malaria being frequent enough even there.

The very complicated ethnography of the region is well described in small space and there are excellent photographs of different racial types. The Thais predominate among the numerous races in the middle and upper regions. The Thais originated in the Yang-tze valley and were pushed south where they populated Burma, Siam, Laos, a part of Upper Tonking and the south of China. They have adapted themselves to life in unhealthy valleys and offer a higher degree of resistance to malaria than other races and groups. At the other extreme are the Miaos who live at altitudes above 800 metres. Their great susceptibility to malaria makes incursions into the lower valleys extremely dangerous. Alongside the Miaos live the Hsiao and the Houns, Chinese mountain tribes who possess a similarly low degree of resistance to malaria.

All the various groups of Thais live in houses built on piles. The space under the dwelling is often used as a stable—an effective measure of zoophily.

In the discussion of this paper it was pointed out that the all important factor to be considered was the distribution of the redoubtable vector *A. minimus* which retains its partiality for feeding on man even in places where domestic animals and game are abundant. The author replied that the distribution of *A. minimus* determines the ethnographic distribution.

Norman White

SAUTET J & MARVENTE H. Contribution à l'étude de l'écologie de divers anophèles vecteurs du paludisme au Liban et au Soudan français. [A Study of the Outdoor Resting Places of some Malaria-carrying *Anopheles*.] *Bull Soc Path Exot* 1943 July 7: 36 Nos 7-8 238-9

The authors report observations on the resting of *Anopheles* of several species in the open outside houses.

In the Lebanon *A. sackrovis* (clausen) has been found several times in caves and holes in trees—there is a considerable daily turn-over for freshly gorged females may be found. *A. sergenti* and *A. superpictus* have been found in holes in walls the former at a time when it could not be found in a very malarious village close by. The authors do not indicate the season at which these observations were made.

At Bamako R. Niger observations were made in August-September (i.e. after the rains but before the height of the dry season). They had no difficulty in discovering adult *A. gambiae* far from human habitations, particularly in folds in bark of the "fromager" (the silk cotton tree, *Croton*). In such places they found adults of both sexes. Some females were gorged, and others were hungry and attacked man. They are in these refuges not only by day but also quite late in the evening. The authors also found mosquitoes of this species in screens made of straw.

They recall the fact that in several parts of the world species of *Anopheles* which are undoubtedly house haunTERS may be found resting in natural environments
P A Buxton

WANSOV M & BERTEAUX M Note sur l'inféctivité de l'*Anopheles* (*Neocellia*) *brunnipes* Theobald [The Infectivity of *Anopheles* (*Neocellia*) *brunnipes* Theobald.] *East African Med J* 1944 Sept v 21 No 9 272-3

Anopheles brunnipes is a mosquito of wide distribution in tropical Africa but has always seemed to be rare. It was originally described from Léopoldville in 1904 and after prolonged search the authors rediscovered it at the same place in 1942. At Léopoldville the adults are only found in the cool dry season (May to August) they occur in labourers huts and are frequently full of blood. In 102 females dissected four salivary infections were found but in view of its rarity *A. brunnipes* is not regarded as an important carrier of *Plasmodium*. Near Léopoldville the breeding places and early stages remain undiscovered
P A Buxton

D ABRERA V St. E The Eggs of the Ceylon Anopheline Mosquitoes. *J Malaria Inst of India* 1944 June v 5 No 3 337-59 18 figs 1 pl & 1 map [22 refs]

This article embodies the results of studies of the external characteristics of the eggs of Ceylon anophelines based on original investigation and a study of the literature. In most cases eggs were obtained in the laboratory from gravid females which laid naturally though in some cases wild eggs found on natural water were used. The species being determined by allowing a proportion of preliminary examination to hatch and by comparison with eggs obtained after dissection from gravid females. This latter method was also used for examination of the texture of the exochorion. A detailed account is given of the mode of oviposition of *A. subpictus*, *A. barbirostris* and *A. varuna*.

Neither original specimens for examination nor previous descriptions were available of the eggs of *A. insulæflorum* or *A. pseudobarbirostris* which remain known and no additional material was available on which to check previous descriptions of *A. annandalei* var *interruptus* or *A. ramsayi*. Eggs of the following species were available and are described: *A. barbirostris*, *A. hyrcanus* var *nigerrimus*, *A. gigas* var *refutans*, *A. aconitus*, *A. varuna*, *A. cf. A. subpictus*, *A. vagus*, *A. tessellatus*, *A. leucosphyrus*, *A. annularis*, *A. jamesi*, *A. maculatus* and *A. karwari*. Descriptions of the eggs of *A. atheni*, *A. gigas* var *refutans* and probably *A. karwari* are original and are given in appropriate detail.

Descriptions given by CHRISTOPHERS and BARRAUD [this *Bulletin* 1932 136] notably in the consistently lower number of float ridges while the *A. barbirostris* agree very closely with the previous authors' description. The differences which have been carefully checked are far consistent to be lightly dismissed and it seems probable that confusion occurred.

A detailed description is given of the eggs of *A. varuna* which differs from that of M. A. U. MENON (*J Mal Inst of India* 1938 v 1 121) notably in the very egg without exception was beautifully and intensely sculptured with polygonal markings distributed over the entire integument. The author considers that considerable confusion prevails and suggests further investigation of the relationship between *A. minimus*, *A. flucialis* and *A. varuna*.

A tendency to the occurrence of polygonal markings on the ventral surface of the eggs of *A. culicifacies* not noted by previous authors is described.

Eggs from specimens of *A. jayakeri* with three banded and four banded palps were examined and consistent differences noted.

In other species the eggs found in Ceylon are similar to those previously recorded and brief descriptions and measurements only are given. The paper includes a key to the eggs of Ceylon anopheline mosquitoes. *G Macdonald*

DAS GUPTA, B. M. & GANGULI, S. K. Developing Gametocytes and Schizonts of *Plasmodium falciparum*—a Case showing all Stages in the Peripheral Circulation. *Indian Med Gaz* 1944 Oct. v 79 No 10 453-9 16 figs. on pl.

The case described is that of a young adult 25 years of age who was admitted to the hospital in Calcutta in an extremely emaciated condition shortly before death. There was a heavy infection with *P. falciparum* which was remarkable in that large numbers of gametocytes in all stages of development were present in the peripheral blood, together with numbers of schizonts the majority of which had been phagocytosed especially by polynuclear leucocytes. The occurrence of developing gametocytes in the blood is most unusual, as these forms are found normally in the internal organs particularly the bone marrow where as the authors remark, they can frequently be demonstrated by sternal puncture when absent from the peripheral blood. An excellent coloured plate depicts the developing crescents and phagocytosed schizonts. *C M Mayon*

KRAV B H & SMITH J A Death due to Estivo-Autumnal Malaria. A Resume of One Hundred Autopsy Cases, 1925-1942. *Amer J Trop Med* 1944 Sept v 24 No 5 317-22

The hundred autopsies on cases of *P. falciparum* malaria represent 1.6 per cent of all the autopsies performed in the Gorgas Hospital Ancon Canal Zone during 17½ years. Sixty per cent of all deaths were followed by post-mortem examination.

Deaths from *falciparum* malaria occurred in all months but were somewhat more numerous in May and June and in December and January than in other seasons. Seventy patients were male 30 female among the Panamanians the sex ratio was equal. These figures reflect the sex distribution of the races on the Isthmus. The average age of the 100 patients was 22.6 years but of the 39 Panamanians in the series 34 were aged 10 years or less. If the Panamanian survives childhood he is unlikely to die of malaria. Peripheral blood parasite density was inadequate as an index of the seriousness of the disease. 29 of 66 patients who died had light infections. Twelve of these died within 24 hours of admission to hospital despite large doses of quinine. The clinical symptoms and pathological changes associated with shock were recorded in one-third of the patients about whom such information was available. The plugging of cerebral capillaries did not appear to be closely related to the occurrence of the symptoms of cerebral malaria. *Norman White*

DÄHRZ G Zur Frage des Verhaltens der Retikulozyten bei den durch Malaria bedingten Anämien. [The Reticuloocytes in the Anaemia of Malaria.] *Dtsch. Tropenmed. Ztschr* 1944 Feb-Mar v 48 No 3-6 49-59 2 figs.

Very high reticulocyte counts have been recorded in malarial anaemia which is of the secondary type and therefore predominantly hypochromic.

The author has investigated the changes occurring in the reticulocyte counts during treatment with (1) atebria followed by plasmoquine (2) atepa.

[(Bayer) tablets contain atebrian 0.1 gm. and plasmoquine 0.005 gm.] and (3) an atebrian like drug. The findings were very similar for all three drugs. Simultaneous estimates were made of the haemoglobin and the blood sedimentation rate.

The atebrian plasmoquine treatment consisted of—atebrian 0.3 gm. daily for three days by the intramuscular route then 0.1 gm. thrice daily by the mouth for three days and plasmoquine 0.01 gm. daily for four days [Elsewhere the dose of plasmoquine is stated to have been 0.01 gm. twice daily for four days.]

There were great variations in the reticulocyte count both before and after the treatment but generally speaking in patients with pronounced anaemia there was a sharp increase in the reticulocytes about a week after the treatment was started a maximum response during the 2nd and 3rd week and a gradual fall towards normal. In patients who were not anaemic the increase in the count was very slight to moderate.

Step by step with the increase in the reticulocytes there was usually a rise in the haemoglobin though occasionally there was a fall when the initial percentage of haemoglobin had been high.

The blood sedimentation rate was initially high in patients with profound anaemia it fell gradually during and after treatment but in non anaemic patients the initial rate was low and not infrequently it rose during treatment. A persistently high sedimentation rate was regarded as suggesting that a relapse was likely to occur.

When iron and vitamin C were administered after the end of the treatment there was usually a further rise in the number of the reticulocytes.

Two graphs illustrate the types of reticulocyte response that were observed.

John W. D. Megaw

STEINBERG L. D. KANIBOLOTSKAYA E. N. & KARLOVA N. S. [Clinical Observations on the Course of Malaria in Children in Voronezh (Aestivo-Autumnal Period of 1943)] *Pediatrics* Moscow 1944 No 3 24-32 5 charts. [In Russian.]

The authors describe atypical phenomena in the course of malaria observed by them among children of the Voronezh province which was one of the theatres of war partly under German occupation in 1941-1943 and had suffered from an epidemic outbreak of malaria. The present observations were based on 154 cases of which 91 represented benign tertian 24 malignant tertian and 5 quartan while in 34 cases a single examination revealed no parasites the diagnosis of malaria being based on clinical data. In all these cases the clinical course of malaria was similar irrespective of the type of infection present. While in half of the patients the paroxysms of fever were typical in the other half they showed various aberrations. Thus there was continuous fever for 3-5 days which was unaffected by the usual doses of quinine and acriquine [mepacrine]. The onset of fever was rarely accompanied by rigor and profuse sweating was rarely observed during the crisis. The duration of the paroxysm as well as the subsequent presence of parasites in the peripheral blood and the occurrence of early relapses were suggestive of a relative degree of quinine- and acriquine-resistance in the patients. The atypical temperature curve and drug resistance sometimes resulted in erroneous diagnosis confusion with typhus fever, which was also prevalent in the country being especially common. While the splenic enlargement was usually typical enlargement of the liver was rarely present. In some of the children suffering from alimentary dystrophy the splenic reaction to malarial infection was suppressed. Marked oedema was observed in 25 cases. Among symptoms unusual in children acute headache associated with malarial paroxysms was noted in most of the cases.

The authors also describe the effect of untreated malarial infection upon various concomitant diseases. Observations on the combined course of tuberculosis and malaria showed that the latter was capable of activating the tuberculous process if the child acquired malaria during the course of the primary infection. Malaria also prolonged the duration of dysentery and pneumonia while in the case of diphtheria, serotherapy proved to be ineffective. In all these cases the treatment of the concomitant diseases began to progress favourably only after administration of quinine.

The authors are inclined to attribute the atypical symptoms observed by them to peculiarities of the malarial parasites. These might be due to the introduction of virulent foreign strains from Italy (by Italian troops) or from Middle Asia (Uzbek troops). On the other hand there may have been an increase in the virulence of local strains, owing to the absence of anti-malarial control and treatment as well as to serial passage of the parasites through undernourished debilitated human hosts.

C. A. Hoare

FITZ HUGH T. Jr. PRYER, D. S. & HORSING, H. U. The Cerebral Form of Malaria. *Bull. U.S. Army Med Dept.* 1944 Dec. No. 83 39-48.

In a U.S. Army general hospital somewhere in India, where malaria is highly endemic, 6,059 patients suffering from malaria were treated during a period of six months. Among them were 140 cases of cerebral malaria, 2.3 per cent. of the total. The patients were of two classes. Group A being composed of American officers and enlisted men (half Negro soldiers) and a few American women, and Group B comprising officers and men of an Allied nation. Group A consisted of carefully selected individuals whose nutritional state was excellent and whose health had not been impaired by malaria or other infestations. Men of Group B had been less carefully selected—most had suffered from repeated attacks of malaria and many harboured intestinal parasites. Group A supplied 1,784 patients of whom two died. Group B 4,293 patients of whom 38 died. There were 40 cases of cerebral malaria in Group A with two deaths and 100 cases in Group B with 33 deaths. The great majority of cerebral cases were *P. falciparum* infections, but one case in Group A was ascribed to *P. vivax* and in Group B four (one being fatal) to *P. vivax* and one to *P. malariae*.

The variable symptomatology of cerebral malaria is well described. One patient in Group B had severe hypoglycaemia. Maintenance of blood sugar at a level compatible with life while quinine suppressed the malaria infection resulted in complete recovery. There was strong reason to believe that malaria was the cause of this hypoglycaemia.

In prognosis the association of convulsions with coma is grave. 80 per cent. of such cases ended fatally. If to these symptoms be added a high peripheral blood parasite density the outlook is all but hopeless. On the other hand a number of fatal cases of cerebral malaria had few or no demonstrable parasites in the peripheral blood.

The great majority of cases of cerebral malaria require one or more intravenous injections of quinine hydrochloride, 0.32 to 0.65 gm. in saline or saline-glucose. The drug well diluted preferably to 500 cc. or more is administered slowly. Doses of quinine as high as 3 or 4 gm. each 24 hours for two or three days are recommended thereafter 2 gm. a day until the patient is out of danger of relapse. In muscular or convulsive patients intravenous sodium amytal is most useful. In coma, spinal drainage may be of value. Blood or plasma transfusions may be of great value in cases with anaemia, shock or pulmonary oedema. [Pulmonary oedema is usually regarded as a contraindication for

transfusion in such cases if fluid is needed LOGAN (*Brit Med J* 1944 Aug 5 181) recommends administration through a Ryle's tube into the stomach.] *Norman White*

MCGINN S & CARMODY J T B Cerebral Symptoms in Malaria. *U.S. Nav Med Bull* 1944 Dec. v 43 No 6 1157-62.

At a base hospital, cerebral symptoms have been the most serious and frequent complication in patients suffering from malaria. Sixteen such cases are described the most surprising feature about them being that they were all ascribed to infection with *P. vivax*. Three of the 16 patients died. In two of these *P. falciparum* was found in addition to *P. vivax* in the remaining 14 only *P. vivax* was present. Eight of the patients had convulsions one had many violent convulsions recurring over a period of nine days. In others a state of coma followed one or more initial convulsive seizures. Fifteen patients were unconscious for a period of from a few hours to five days the other dying suddenly in his second convulsion. The intravenous injection of quinine was necessary in 15 of the patients generally 15 grains in 1 000 cc of 5 per cent dextrose solution. One such injection was sufficient in six patients the others requiring two or more. The post-mortem examination of the fatal cases failed to reveal pigmentation and capillary thromboses in the brain two of them were icteric.

A case of quinine sensitivity is reported which was revealed only after the intravenous injection of quinine had been begun. Complete heart block and ventricular fibrillation ensued after only three grains of quinine had entered the vein. The prompt intravenous injection of adrenaline (1 cc. of 1 : 1 000 solution) averted the threatened fatality *Norman White*

KERN R. A & NORRIS R F Liver Involvement in Malaria. *U.S. Nav Med Bull* 1944 Nov v 43 No 5 847-58.

Clinical experience based on the treatment of 1 153 cases of malaria in a hospital ship impressed the authors with the frequency of involvement of the liver in all types of malaria infection and in all stages of the disease. Enlargement of the liver was noted in 59 of 100 consecutive patients suffering from malaria. The enlargement varied from 1 to 2 to 5 or 6 cm below the costal margin in the midclavicular line. The frequency of enlargement was higher in *falciparum* than in *vivax* infections. Evident jaundice was rarely noted but the van den Bergh reaction frequently gave abnormal readings. In 16 out of 21 patients with enlarged liver and fever the bilirubin exceeded 0.5 mgm per 100 cc. of serum. This limit was exceeded in 6 out of 12 patients with enlarged liver but no fever in 7 out of 16 with fever but no enlargement of liver and in only 3 out of 12 with neither enlargement of liver nor fever. The results of the bromsulphalein test in 19 patients were in general accord with the van den Bergh reactions. Enlargement and altered function of the liver are as common in the primary attack as in subsequent attacks they are not evidence of chronicity. The nature of the liver change is uncertain it may be a swelling of the parenchymal cells with compression of the sinusoids malarial pigment may be found in the Kupffer cells *Norman White*

MILCALF R. J & UNGAR J Jr Relapsing Malaria, Analysis of Cases from the Solomons *U.S. Nav Med Bull* 1944 Nov v 43 No 5 859-70

The observations recorded concern 250 men who had been invalided back to the United States after having been infected with malaria in the Solomons. Records show that many if not most of these men were originally infected

The authors also describe the effect of untreated malarial infection upon various concomitant diseases. Observations on the combined course of tuberculosis and malaria showed that the latter was capable of activating the tuberculous process if the child acquired malaria during the course of the primary infection. Malaria also prolonged the duration of dysentery and pneumonia, while in the case of diphtheria, serotherapy proved to be ineffective. In all these cases the treatment of the concomitant diseases began to progress favourably only after administration of quinine.

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At a base hospital, cerebral symptoms have been the most serious and frequent complication in patients suffering from malaria. Sixteen such cases are described the most surprising feature about them being that they were all ascribed to infection with *P. vivax*. Three of the 16 patients died. In two of these *P. falciparum* was found in addition to *P. vivax* in the remaining 14 only *P. vivax* was present. Eight of the patients had convulsions one had many violent convulsions recurring over a period of nine days. In others a state of coma followed one or more initial convulsive seizures. Fifteen patients were unconscious for a period of from a few hours to five days the other dying suddenly in his second convulsion. The intravenous injection of quinine was necessary in 15 of the patients generally 15 grains in 1 000 cc. of 5 per cent dextrose solution. One such injection was sufficient in six patients the others requiring two or more. The post-mortem examination of the fatal cases failed to reveal pigmentation and capillary thromboses in the brain two of them were icteric.

A case of quinine sensitivity is reported which was revealed only after the intravenous injection of quinine had been begun. Complete heart block and ventricular fibrillation ensued after only three grains of quinine had entered the vein. The prompt intravenous injection of adrenaline (1 cc. of 1 1 000 solution) averted the threatened fatality. *Norman White*

KERN R. A. & NORRIS R. F. *Liver Involvement in Malaria. U.S. Nav Med Bull.* 1944 Nov. v 43 No 5 847-58.

Clinical experience based on the treatment of 1 153 cases of malaria in a hospital ship impressed the authors with the frequency of involvement of the liver in all types of malaria infection and in all stages of the disease. Enlargement of the liver was noted in 59 of 100 consecutive patients suffering from malaria. The enlargement varied from 1 to 2 to 5 or 6 cm. below the costal margin in the midclavicular line. The frequency of enlargement was higher in *falciparum* than in *vivax* infections. Evident jaundice was rarely noted but the van den Bergh reaction frequently gave abnormal readings. In 16 out of 21 patients with enlarged liver and fever the bilirubin exceeded 0.5 mgm. per 100 cc. of serum. This limit was exceeded in 6 out of 12 patients with enlarged liver but no fever in 7 out of 18 with fever but no enlargement of liver and in only 3 out of 12 with neither enlargement of liver nor fever. The results of the bromsulphalein test in 18 patients were in general accord with the van den Bergh reactions. Enlargement and altered function of the liver are as common in the primary attack as in subsequent attacks they are not evidence of chronicity. The nature of the liver change is uncertain it may be a swelling of the parenchymal cells with compression of the sinusoids malarial pigment may be found in the Kupffer cells. *Norman White*

METCALF R. J. & UNGAR, J. Jr. *Relapsing Malaria, Analysis of Cases from the Solomons. U.S. Nav Med Bull.* 1944 Nov. v 43 No 5 859-70.

The observations recorded concern 250 men who had been invalided back to the United States after having been infected with malaria in the Solomons. Records show that many if not most of these men were originally infected

with *P. falciparum* but on their arrival in the United States *P. m. ax* infections were found in every case and *P. falciparum* was not once observed. The group consisted of individuals almost completely lacking in the ability to acquire an adequate degree of immunity and the relapse rate was very high in spite of what is generally considered to be very adequate malaria treatment. Atabrine (mepacrine) was remarkably ineffective in the treatment of these cases, though it was given in large doses. The last course of treatment previously received by all but two of these patients comprised 3.3 gm. of atabrine. Large doses of quinine were much more effective. The smallest doses of quinine used were 15 grains thrice daily for five days then 10 grains thrice daily for five days, then 15 grains daily for six weeks. Little was gained by the combination of quinine and atabrine. There was no evidence that plasmoquine was of value. At first, neourphenamine was used in conjunction with quinine. It made the patient feel better but had insufficient influence on the relapse rate to warrant its routine use. The ideal drug for eradicating plasmodia, particularly the latent form recently termed the cryptozoit, may well be found to be a colloidal plasmocicide having a special affinity for the reticulo-endothelial system. At this writing such a compound has been evolved by combining high molecular pectin solutions with various soluble plasmocides. Toxicity studies are promising but as yet no opportunity for using the substance in experimental malaria has been afforded.

The morphology of *P. m. ax* seen in these cases was unusual in certain respects. Multiple infection of red cells was common—double rings were seen in many smears, triple rings in occasional smears and four rings in a single cell were seen five times. There was no doubt that these trophozoites were *P. m. ax* and not *P. falciparum*. Intermediary forms between young trophozoites and adult gametocytes are described. During the examination of hanging drop preparations of malarial blood motile forms were seen free in the plasma. These were rod-shaped and had a highly refractile spherical body which could shift its position from one end of the rod to the other. On impact with a red cell the rod would split in its long axis, the two resultant portions ballooning out to form a perfect ring. It is possible that these forms were merozoites from ruptured red cells.

A very low parasitaemia was capable of producing a severe rigor and no appreciable increase of parasite density was noted in successive relapses in the same individual.

Norman White

LANCET 1945 Feb 3 144-5 Determination of Plasma Mepacrine. A Note on the Anticoagulant. From the Army Malaria Research Unit. [Reprinted by kind permission]

Several methods have recently been published for the determination of mepacrine in plasma (Brodie and Udenfriend 1943; Masen 1943). These authors recommend the use of oxalate as an anticoagulant but it has now been found that if ammonium oxalate or any salt mixture containing ammonia (e.g. Wintrobe's salt mixture) is used as the anticoagulant the amount of mepacrine found in the plasma is greatly increased.

The mean plasma mepacrine concentration of the patients from each of three hospitals has been determined by a modification of the method of Masen (1943). The table gives the mean plasma mepacrine concentration at the end of 48 hours therapy—i.e. after 1.6 g. mepacrine. It is seen that there was no significant difference between the mean plasma levels of the patients of hospitals A and B and that neither differed significantly from that of an experimental group of medical students and research-workers who had been given the same dosage under controlled conditions. The mean plasma level of patients from

Plasma Mepacrine of Patients after taking 16 g Mepacrine in 48 Hours

	No. of patients	Mean plasma mepacrine ($\mu\text{g/l}$)	SE mean
Hospital A	72	84	± 5
Hospital B	6	96	± 19
Hospital C	16	245	± 17
Experimental group	6	81	± 9
Hospital C (after changing oxalate)	4	88	± 10

hospital C was however nearly three times as great. The difference was maintained throughout the whole of the therapy course. Wintrobe's salt mixture was used as the anticoagulant at hospital C. On changing the anticoagulant to potassium oxalate similar figures were obtained from this hospital also.

In vitro experiments have shown that the increase in plasma mepacrine concentration was due to the ammonia in the Wintrobe salt mixture. The ammonia presumably displaces mepacrine from the white blood-cells which have a high concentration of the drug (Brodie and Udenfriend 1943). It has also been shown that if sodium citrate or heparin is used as the anticoagulant the concentration of mepacrine in the plasma is the same as with potassium oxalate.

Conclusions and summary.—If the anticoagulant used contains ammonia the concentration of mepacrine in the plasma from subjects receiving the drug is much greater than that observed when the plasma is prepared with anticoagulants not containing it. Therefore ammonium oxalate or any salt mixture containing ammonia (e.g. Wintrobe's salt mixture) must not be used as an anticoagulant in the preparation of the plasma for mepacrine determinations. Potassium oxalate, sodium citrate or heparin are satisfactory anticoagulants.

References

- BRODIE B B & UDENFRIEND S (1943) *J Biol Chem* v 151 289-317
 MARRIS J M (1943) *Ibid.* v 148 529-36

SHANNON J A, EARLE D P Jr, BRODIE B B, TAGGART J V, BERLINER R. W *et al*. The Pharmacological Basis for the Rational Use of Atabrine in the Treatment of Malaria. *J Pharm & Exper Therap* 1944 Aug v 81 No 4 307-30 2 figs [11 refs.]

(1) The physiological disposition of mepacrine (atabrine) in the body

The chief features of this are rapid complete absorption from the gastrointestinal tract, a low rate of excretion, a low rate of degradation, and a tendency to extensive localization in many organs of the body. In the work described the mepacrine was extracted by ethylene dichloride and the extract was washed with alkali [BRODIE & UDENFRIEND this *Bulletin* 1943 v 40 821].

Distribution in the blood.—In the blood the concentration of mepacrine in the erythrocytes is 1-2 times that in the plasma, and the concentration in the leucocytes is over 200 times that in the plasma. The ratio between the concentration in whole blood and that in the plasma varies considerably at different times, partly because of variations in the leucocyte count, partly because of factors at present unknown. When blood is shed much mepacrine is released from the leucocytes into the plasma, consequently the true concentration in the plasma can be determined only if the blood is centrifuged at high speed directly after withdrawal. About 80-90 per cent. of the mepacrine

in the plasma is bound to the plasma proteins and only 10-20 per cent. is in true solution in the plasma water—it is this 10-20 per cent. which is presumably in equilibrium with the extracellular fluid of the tissues. Technical reasons make the determination of the concentration in plasma water very difficult

PLASMA ASPIRIN CONCENTRATION: micrograms/liter

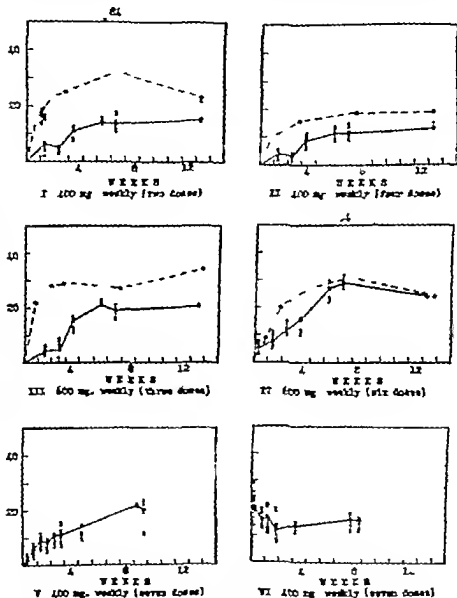


FIG. 1.—Weekly minimal and maximal plasma mepecaine concentrations observed during various regimes of suppressive thepaquine therapy.

The mean weekly maximal concentrations are indicated by large dots the individual values by small dots. The mean weekly maximal concentrations are indicated by open circles. Note should be taken of the fact that the number of individuals in each group is too small to delineate the mean concentrations accurately. The data do however reflect the trend which is to be expected on each of the regimes studied.

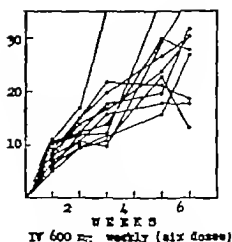
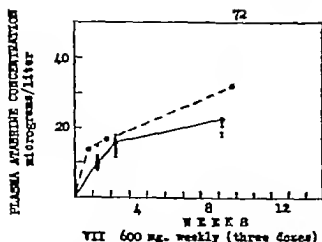


FIG. 2.—Weekly minimal and maximal plasma mepacrine concentrations during the administration of 600 mg. mepacrine dihydrochloride weekly. The symbols used are the same as in fig. 1.

FIG. 3.—The weekly minimal plasma mepacrine concentrations observed in the individuals of a group receiving 600 mg. of mepacrine dihydrochloride weekly in six 100 mg. doses administered on six consecutive days each week. [Reproduced from the *Journal of Pharmacology and Experimental Therapeutics*]

consequently the authors recommend that all investigations should be based upon the concentration of mepacrine in whole plasma.

Distribution in the body—Mepacrine was given to dogs which were killed after various periods. In a dog killed after 14 daily doses of 20 mgm. per kgm. the concentration of mepacrine in microgram per litre was 0.06 in the plasma, 55 in the muscle, 310 in lung, 571 in spleen and 1,300 in liver. After single intravenous injections equilibrium took more than four hours to reach. In man there is a similar localization of mepacrine in the tissues, only small fractions remaining in the plasma. Excretion in the dog and in man does not account for more than 1–5 per cent of the daily dose, thus patients receiving 300 mgm. daily excreted each day about 5–13 mgm. in the urine and about 10–30 mgm. in the faeces. Degradation or katabolism of mepacrine is also slow and apparently it depends upon the concentration in the plasma. On a daily dose mepacrine gradually accumulates in the body until eventually equilibrium is reached at the point where disposal (degradation plus excretion) balances intake. The level at which this equilibrium occurs differs in different individuals.

(2) Evaluation of mepacrine suppressive therapy by study of plasma concentrations achieved on various dosage schedules

Groups, each of about 10 young healthy men, were given mepacrine according to the following schedules—

- (1) 200 mgm. on Tuesdays and Thursdays
- (2) 100 mgm. on four days of the week
- (3) 200 mgm. on three consecutive days in the week
- (4) 100 mgm. on six days of the week
- (5) 50 mgm. on six days of the week and 100 mgm. on Sundays
- (6) 200 mgm. on five consecutive days at the beginning of the course (loading doses) and then 400 mgm. weekly as in (5)
- (7) 200 mgm. on Mondays, Wednesdays and Fridays.

Samples of blood were taken at times when the concentration in the plasma might be expected to be minimal and maximal respectively.

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The resulting mean concentrations of mepacrine in the plasma are shown in the accompanying graphs. It will be seen that on these dose schedules the plasma concentration rises gradually during a period of approximately six weeks and then reaches a comparatively steady level. This level is lower with a weekly dose of 400 mgm. than it is with a weekly dose of 600 mgm. The degree of protection against malaria presumably depends upon the level of the plasma concentration so that it is lower in the early weeks than later and lower with 400 mgm. weekly than with 600 mgm. weekly. The level of plasma concentration finally reached depends more upon the total amount of the drug received per week than upon the exact arrangement of doses within the week. An adequate level of plasma concentration can be reached more quickly by initial "loading" doses (régime 6) than by giving a uniform dosage throughout. There is considerable individual variation in the plasma concentration of mepacrine reached in any given dose-schedule. It is believed that the plasma concentration of mepacrine required to prevent clinical malaria is about 20 microgm. per litre.]

(3) Plasma concentrations of mepacrine during several régimes of mepacrine therapy

Patients suffering from malaria were given mepacrine according to various régimes and daily estimations were made of the concentration of the drug in the plasma. The average figures (calculated from the authors' tables) are reproduced below.

In the patients treated by course 2 the plasma concentration was 640-1100 micrograms per litre after 20 minutes and 400-800 micrograms three hours later. Two out of six patients showed severe toxic symptoms (depression of respiration and mild convulsions) during this period. Up to 0.4 gm. mepacrine may be injected intravenously without symptoms provided it is given slowly but the procedure is not recommended for routine use. With course 3 (there was much individual variation, but a high concentration was reached within three hours after an intramuscular injection of 0.4 gm. mepacrine 0.1 gm. i.d.s. by mouth seldom maintains a plasma concentration greater than that produced by an intramuscular injection of 0.4 gm. With course 4 after several days the plasma concentration tends to become stabilized at 50-100 micrograms per litre. With course 5 most patients remained free from gastro-intestinal disturbances in spite of the high dosage. In cases where oral administration is not at first possible a high concentration may be maintained in the plasma by intramuscular injections of 0.4 gm. initial 0.2 gm. at 8-hour intervals for 2-3 doses, and then 0.2 gm. at 12-hour intervals until oral administration becomes feasible. Following oral administration of mepacrine in the above régimes no severe toxic manifestations were encountered apart from several psychoses which may not have been due to mepacrine since the patients were neurosophistic. Severe toxic reactions occurred in two patients given mepacrine intravenously, and this procedure is not recommended.

The conventional therapeutic course of mepacrine (course 1 above) is criticized as being unsatisfactory since the plasma concentration does not reach satisfactory levels till the fifth day. In a rational chemotherapeutic régime (as exemplified by the use of sulphonamides) sufficient drug should be administered at the time of diagnosis of a disease to obtain the desired blood concentration and the latter should then be maintained by the serial administration of smaller doses e.g., courses 3, 4 and 5. The régime recommended for general use is one in which 0.8 gm. is given on each of one or two days and then 0.3 gm. daily. Unless it is certain that the gastro-intestinal tract is in good condition the authors recommend commencing treatment by an intramuscular injection of 0.4 gm., followed by 0.1 gm. orally at intervals during the first day. In their experience

Course	Dose schedule	Plasma Mepacrine concentration (micrograms per litre)													
		Hours		Days after beginning therapy											
		3	24	2	3	4	5	6	7	10	12	14			
1*	0.5 gm. intravenously rapidly plus 0.5 gm. intravenously slowly	390-790 mean 668	171-428 mean 281	111-217 173	—	82-166 121	—	—	50-117 88						
2	0.1 gm. t.d.s. orally 6 days	—	12-24 mean 17	27-43 33	29-74 42	40-53 45	29-75 65	51-80 61							
3	0.4 gm. intramuscularly plus 0.1 gm. by mouth followed by 0.3 gm. orally distributed throughout the next 12 hours and then (a) 0.1 gm. b.d.s. by mouth for 5 days or (b) 0.1 gm. t.d.s. by mouth for 5 days	51-155 mean 98	34-121 mean 61	35-121 60	29-115 64	33-135 74	41-143 69	44-109 76							
4	0.2 gm. by mouth 4 times in one day and then 0.1 gm. t.d.s. for 5 days	—	19-124 mean 60	25-120 63	28-102 63	29-112 68	40-160 70	35-121 63	38-66 59						
5	0.2 gm. by mouth 4 times a day for 2 days and then 0.1 gm. t.d.s. for 12 days	—	43-140 mean 73	47-171 106	52-135 92	48-147 89	50-130 86	58-105 85	57-109 61	44-120 95	46-127 89	64-180 100			

In course 1 whole blood concentrations are given as at the time the chemical method of measuring mepacrine in plasma was not sufficiently refined. In courses 2 to 5 the plasma mepacrine concentrations are given. The ratio between whole blood concentration and plasma concentration is not altogether constant but approximately the concentration in whole blood is four times the value for plasma.

intramuscular injection of mepacrine dihydrochloride is not attended by sufficient local discomfort to contraindicate it.

[This is a most important paper laying the foundations for a rational method of administering mepacrine, and it deserves careful study in the original. It should be remembered, however that the accuracy of estimations of plasma mepacrine is low]

F. Hacking

CHEN G & GEILING E. M. K. Observations bearing on the Mechanism of the Elimination of Quinine and Atebrin from the Circulation and Tissues. *J. Pharm. & Exper. Therap.* 1944 Oct v 82, No 2, 120-32, 9 figs [10 figs.]

The present investigation was undertaken to find out the reason for the rapid disappearance of quinine and atebrin from the circulation or tissues after injection. HATCHER and WEISS [this *Bulletin* 1927 v 24 273] believed that quinine was fixed by the capillaries. In the case of atebrin HÄCHT [this *Bulletin* 1937 v 34 157] noted that it was taken up by the organs with which it first came in contact and concluded that its location depends therefore on the route of administration. It had already been shown by LIPKIN and by KELSEY and OLDFHAM [this *Bulletin*, 1920 v 15 127 1944 v 41 260] that destruction of quinine in tissues takes place largely by enzyme action. The manner in which atebrin is metabolized has not yet been determined.

In the present experiments chickens were used after partial blockage of the R.E. system by 1 per cent. "norit" (activated carbon) in physiological agar; dogs were used with hepatic injury from administration of Cl_4 , rabbits with leucopenia as the result of exposure to nitro-mustard gas as well as after evisceration, and heart-lung preparations of this animal were also used. By these means it could be determined whether the R.E. system, the blood elements of bone marrow or the capillary wall play a part in the early elimination of the drugs. Estimations of the amount of each drug present in circulation and tissues were made up to two hours after intravenous administration.

A simple accurate and rapid fluorimetric method was developed for the estimation of quinine alone in blood and tissues by digesting with 2 per cent. NaOH followed by extraction with ethylene dichloride. In the estimation of quinine along with its fluorescent degradation products digestion with NaOH was omitted. Suitable standards were employed [for details of estimation the original must be consulted]. Atebrin was estimated by a slight modification of the method of BRODIE and UDEVEREND [this *Bulletin* 1944 v 41 453].

On injecting quinine or atebrin intravenously in the chick, rabbit and dog it was found that 95 per cent. had left the circulation within 3 minutes and the same was approximately true for heart-lung preparations. After one hour the amount of each present was very small. The rate of disappearance was the same in normal animals as after the experimental procedures described above.

Quinine degradation products accounted for 10-12 per cent. of the fluorescent material in the circulation of chicks and rabbits one hour after administration. 70 per cent. of the quinine injected was destroyed in five minutes in heart-lung preparations whereas in the case of atebrin 80-90 per cent. of the amount administered was found in the lung up to two hours after injection the remainder being in the blood and heart. These results show that atebrin was but slowly metabolized in the tissues in question, while quinine was rapidly destroyed by enzyme action, a fact which was confirmed by *in vitro* experiments.

The relationships between the differences in blood levels of the drugs and the times after administration at which they were estimated, suggest that the early rapid removal of these drugs from the circulation is due to an adsorption process

in the tissues. It was concluded that the site at which adsorption takes place is the capillaries and chiefly those of the lung
J D Fulton

HAMMICK D L. & CHAMBERS W E. Optical Activity of Excreted Mepacrine
[Correspondence.] *Nature* 1945 Feb 3 141

YARYGIN N E & NAGIBINA N I [On the Treatment of Malaria in Children by Intramuscular Injections of Acriquine and the Role of C.S.F. "Towing" in the Treatment of Malaria Cases Refractory to Acriquine-Quinine] *Pediatrics* Moscow 1944 No 3 32-8 [In Russian]

Acriquine [=atebrin=mepacrine] therapy is now recognized in the Soviet Union as the standard method of treatment of malaria. Although its effectiveness is beyond doubt one occasionally meets with complaints that acriquine does not always suppress the paroxysms in children. According to the authors this impression is due to the fact that owing to its unpleasant taste children are reluctant to take the drug or they take an incomplete dose and furthermore they are subject to vomiting in the course of which the drug is expelled. The authors found that all children suffering from malaria irrespective of its type could be effectively treated by intramuscular injection of a 4 per cent solution of acriquine hydrochloride in doses corresponding to the age of the patient. The total number of cases thus treated was 410 (398 benign tertian 9 malignant tertian and 9 quartan)

Among these there were a number (2.2 per cent.) of acriquine- and quinine-resistant cases. In these injections of 4 per cent acriquine were combined with treatment by what is described as "towing" of the cerebrospinal fluid in the course of which a lumbar puncture is done and the first 3-5 cc of c.s.f. are removed after which a syringe barrel with a capacity of 5 cc is attached to the needle and quantities of 4-5 cc. of c.s.f. are alternately withdrawn and injected back from 5 to 15 times in succession. This treatment is said to have resulted in the successful cure of drug resistant cases. The method itself is based on the views of A. D. SPERANSKY one of I. P. PAVLOV's collaborators according to which pathological processes and drug-action are controlled by the nervous system. The "towing" of the c.s.f. is said to represent a peculiar form of nervous stimulation (massage) which provides the organism with a nervous background required to render the drug effective.
C A Hoare

FINDLAY G M. & STEVENSON A C. Investigations in the Chemotherapy of Malaria in West Africa. II. Malaria Suppression—Quinine and Mepacrine *Ann. Trop. Med. & Parasit.* 1944 Dec. 30 v 38 Nos 3 & 4 168-87 5 charts [19 refs.]

An interesting historical introduction to this report refers to the experience of expeditions in West Africa mostly during the nineteenth century. These provided evidence that the administration of cinchona bark or quinine is of value in suppressing clinical attacks of West African malaria. The main body of the report is concerned with observations on the efficacy of mepacrine as a malaria suppressive.

When British troops arrived in West Africa in 1940 all ranks were ordered to take 5 grains of quinine daily. There was some opposition to the measure based partly on the groundless belief that quinine may cause sterility and dental caries. A daily dose of 5 grains of quinine is not a highly efficient malaria suppressive but it does prevent clinical attacks in a large number of persons. A daily dose of 8-10 grains is more efficient but it may cause deafness, buzzing in the ears and depression. After changing from quinine to mepacrine prophylaxis many persons felt more alert and active both mentally and physically.

[May 1945]

Two tablets of 0.1 gm. mepacrine a week were insufficient to suppress malaria. During three weeks of May 1942, the incidence of malaria among 600 men receiving such small doses was 155 per 1 000 as compared with 64.8 per 1 000 among 648 men similarly situated who were receiving each 5 grains of quinine a day. On June 1st the dose of mepacrine was increased to 0.4 gm. weekly and the test was continued to November 8th. The incidence of malaria among mepacrine takers was 412.4 per 1 000 as compared with 651.7 per 1 000 among troops taking 5 grains of quinine a day. These are the combined results of observations made in Nigeria, Gold Coast, Sierra Leone and the Gambia.

In 1943 three different groups of Europeans in the same area had different suppressive treatments. Each group consisted of from 2,000 to 3 000 persons the living conditions of all three were similar. Group A received 5 grains of quinine daily, group B 0.4 gm. of mepacrine weekly in two doses, group C 0.1 gm. of mepacrine daily except on Sundays. The malaria rate in group A was much higher than in the other two groups. Group C had the lowest rate.

In 1943 the whole Command were given 0.6 gm. of mepacrine weekly. The clinical malaria incidence is compared with that of the previous year when the mepacrine dose was 0.4 gm. a week. The malaria rate per 1 000 men-days exposure to infection fell in all four colonies from 2.00 to 1.89 in Nigeria, from 2.09 to 1.29 in Gold Coast from 1.50 to 1.15 in Sierra Leone and from 3.95 to 1.13 in the Gambia. All possible causes of the decreased incidence are considered and it is concluded that the increased dose of mepacrine was the most potent factor.

Experience has shown that when changing from quinine to mepacrine prophylaxis it is essential to continue 5 grains of quinine daily until at least 0.6 gm. of mepacrine have been taken otherwise the first two weeks of mepacrine prophylaxis are apt to be marked by a considerably increased prevalence of clinical malaria. It is also essential to begin taking mepacrine 7-10 days before arriving in a hyperendemic zone.

In every case of cerebral malaria that occurred subsequent to the use of mepacrine as a suppressive there was a history that mepacrine either had not been taken or had been taken irregularly. Mepacrine is much less likely to precipitate an attack of blackwater fever than is quinine. During the year quinine was used as a suppressive there were 122 cases of blackwater fever in the Command in the following year when mepacrine had replaced quinine there were but 33 cases. The difference was not associated with any great change in the strength of the Command.

Gastro-intestinal symptoms may occur in a considerable proportion of persons during the first two or three weeks of mepacrine suppressive treatment. The symptoms generally tend to disappear in about 0.2 percent of persons vomiting, epigastric pain and diarrhoea persist. No toxic reactions definitely due to the cumulative action of mepacrine had been recorded in patients taking 0.6 gm. of mepacrine a week for periods up to one year. No increased resistance to mepacrine therapy was shown by patients who had taken mepacrine as a suppressive. Some evidence is given that mepacrine may have a sporozoitocidal action in *falciparum* malaria.

FINDLAY G. M., MARKSON J. L. & HOLDEN J. R. Investigations in the Chemotherapy of Malaria in West Africa. III. Further Investigations on Treatment with Quinine and Mepacrine. *Ann Trop Med & Parasit* 1944 Dec. 30
1: 38 Nos. 3 & 4 201-4

In a previous paper the authors had demonstrated the superiority of a large initial dose of mepacrine over the usual daily dose of 0.3 gm. in the treatment of European patients infected with West African strains of *P. falciparum* and

had shown that mepacrine compared favourably with quinine in the treatment of such patients [this *Bulletin* 1945 v 42, 6]. This further contribution records the results of treatment of 80 more patients suffering from *falciparum* malaria 40 with quinine—30 grains a day for six days—and 40 with mepacrine—0.8 gm the first day 0.4 gm the second and third days and 0.3 gm on each of the next three days. Thick blood films were examined morning and evening. The absorption of quinine was verified by Tanret's test thrice daily.

There was a wide variation in the initial parasite counts in these patients there were more heavy infections in the mepacrine series. There was no significant difference in the response to the two treatments. Mepacrine with a big initial dose can deal with heavy infections by *P. falciparum* as effectively as can quinine. Slight abdominal colic and diarrhoea occurred occasionally during mepacrine therapy but in no case was it necessary to suspend treatment. The patients had all been receiving mepacrine 0.1 gm. daily as a suppressive. All patients on quinine showed a positive Tanret reaction. *Norman White*

BRAUN K. & DE VRIES A. Plasmochin and Quinine as the Cause of Acute Haemolytic Anaemia. *Harefuak* Jerusalem. 1944 Dec. 15 v 27 No 11 [In Hebrew 218-21 English summary 221]

THIRLBY R. L. Hemoglobinuria following Plasmochin Therapy. *U.S. Nav. Med. Bull.* 1944 Dec. v 43 No 6 1232-5

SHISHLAIEVA MATOVA L. S. [Gamostatic Efficiency of Quinolone No 31 in Benign and Malignant Tertian Malaria.] *Med. Parasit. & Parasitic Dis.* Moscow 1943 v 12 No 6 22-32 [In Russian]

The author investigated the duration of the gamostatic effect (i.e. the power to inhibit the development of gametocytes in the mosquito) of a single dose of 0.06 gm of Quinolone No 31. [See this *Bulletin* 1939 v 38 687 in that Russian paper its formula was given as 6-methoxy 8-diethylamino-methylpropylaminoquinoline (methylene bisalicylate).]

The tests were carried out with *Anopheles maculipennis sacharovi* which were fed on cases harbouring gametocytes both before and after administration of the drug. In these experiments there were 23 patients with benign tertian (1,243 mosquitoes) and 28 cases of malignant tertian (1,804 mosquitoes) all of whom were at the same time having a course of treatment with acridine [mepacrine or atabrin]. In addition to these six cases of B.T. and seven of M.T. were treated with plasmocide [plasmoguinine] for comparison with quinoline. The examination of mosquitoes for developmental stages of the malaria parasites showed that both in benign and in malignant tertian malaria a single dose of quinoline had a pronounced gamostatic effect lasting five days which compares favourably with plasmocide. *C. A. Hoare*

METCALF R. L. & HESS A. D. The Relation of Particle Size to the Effectiveness of Paris Green used in Airplane Dusting for Mosquito Control. *Pub. Health Rep.* Wash. 1944 Nov 10 v 59 No 45 1458-65 3 figs. (2 on 1 pl.)

About two-thirds of the total cost of airplane dusting on the reservoirs of the Tennessee Valley Authority is the cost of the paris green larvicide. Only about 25 per cent of the amount of paris green released reaches the treatment area—winds and propeller torque dissipate the rest. Studies were therefore carried out to determine whether an increase in the particle size of the dust would increase the efficiency of airplane dusting. The average maximum diameters of particles ingested by first to fourth instar *A. quadrimaculatus*

[May 1945]

Larvae were 29-51-68 and 106 microns respectively. A special pans green was obtained, 84 per cent. by weight of which consisted of particles of from 20 to 50 microns in diameter as compared with 48 per cent. in the standard pans green in use. The use of this coarse dust resulted in a 60 per cent. increase in the amount of dust reaching the treatment area. Field tests with the coarse dust gave a larval kill of 80-100 per cent. It is recommended that specifications for pans green to be used in airplane dusting should be revised.

DELANEY Anna D & MORRISON D B On the Preparation and Properties of Antigens from *Plasmodium knowlesi* *Am J Trop Med* 1944 Sept., v 24 No 5 323-6 Norman White

In earlier paper the first author with others has shown that a saline extract of *Plasmodium knowlesi* is a reliable antigen for use in complement fixation tests for malaria this Bulletin 1941 v 38 411 1943 v 40 11 In the present report the results of using other types of parasite extracts are given. These extracts are (1) Phosphate buffer extracts of wet and dried parasites (2) Barbiturate buffer extracts of wet and dried parasites (3) Solutions of parasites obtained by treatment with barbiturate and NaOH (4) NaOH solutions of parasites. The method of preparing these four extracts is separately described, as also the technique of their application to the complement fixation test. It was found that phosphate or barbiturate buffer extracts are six to eight times more active than the saline antigens previously employed. The sodium hydroxide solutions are not satisfactory antigens because of their anti-complementary properties. It has been shown that dehydration of phosphate buffer extracts which may be carried out without loss of potency may afford a satisfactory means of storing malaria antigen. Evidence has been produced suggesting that the antigen is a lipid protein complex, but a carbohydrate factor has not been entirely eliminated. C M Warren

JEFFERY G M Investigations on the Mosquito Transmission of *Plasmodium falciparum* Coggeshall, 1935. *Am J Hyg* 1944 Nov v 40 No 3 251-63. 16 refs.

The feeding of the four mosquitoes *Aedes albopictus*, *Aedes aegypti*, *Anopheles gambiae*, and *Culex pipiens* on ducks infected with *Plasmodium falciparum* led to the infection of the first three and of these the *Anopheles* were heavily infected. When fed on clean ducks the mosquitoes infected only 52 and of the 31 only three contracted infections which could be termed satisfactory with 1 000-3 000 and 11 000 parasites per 10 000 red blood corpuscles. In the other ducks the parasites never exceeded 300 per 10 000 red blood corpuscles. This resistance of ducks to mosquito-transmitted infection contrasts very markedly with their susceptibility to infection produced by blood inoculation. As *P. falciparum* was originally discovered in a pheasant, attempts were made to infect pheasants known to be highly susceptible to blood inoculations by means of mosquitoes. The results were similar to those obtained with ducks. It is suggested that the duck is an abnormal host for the parasite and is unsuitable for the satisfactory development of the stages of parasite which must follow the introduction of sporozoites and precede the erythrocytic cycle. Exoerythrocytic stages of development have never been found in hosts of *P. falciparum* but the fact that infections do follow the inoculation of sporozoites suggests that some must be present but in numbers too small to be detected. C M Warren

COATNEY G. R. & COOPER W. C. The Prophylactic Effect of Sulfadiazine and Sulphaguanidine against Mosquito-borne *Plasmodium gallinaceum* Infection in the Domestic Fowl (Preliminary Report) *Pub Health Rep* Wash 1944 Nov 10 v 59 No 45 1455-8

As a result of experiment SIMTON *et al* [this *Bulletin* 1939 v 36 925] concluded that the sulphonamide prosectasine had some action as a true causal prophylactic against mosquito-borne infections of the Rumanian strain of *P. falciparum*. It is well known that other sulphonamides possess therapeutic properties in various types of malaria. The present authors have tested the prophylactic effect of sulphadiazine and sulphaguanidine in mosquito-borne infections of *P. gallinaceum* and this note is a preliminary report of their results.

White Rock chicks 3-7 days old were used as hosts. One infected *Aedes aegypti* mosquito afterwards shown by dissection to have sporozoites in its salivary glands was allowed to feed on each bird between the first and second doses of the drug which was given by mouth twice daily. Blood smears were made of all the experimental birds each day starting from the sixth while brain smears were examined after death for the presence of exoerythrocytic forms. In one experiment 24 chicks were used, each of which was bitten by an infected mosquito. Eight birds received sulphadiazine and eight sulphaguanidine in doses of 1.0 mgm per gm. of body weight twice daily by mouth for eight days. The remaining eight birds acted as controls. The blood of the drug treated birds and of one control was parasite-free at the end of 35 days. The other controls died from infection between the 10th and 16th days. Subinoculation of the blood of the survivors to fresh birds demonstrated the absence of infection and this was confirmed when the survivors were themselves reinoculated with heavily parasitized blood, as all died from the resulting infection whereas the course of infection in a chronically infected bird inoculated at the same time was unaltered. A second experiment with both drugs yielded similar results with sulphadiazine but in the case of 12 birds treated with sulphaguanidine two had parasites in their blood on the 18th and 20th days after exposure while the others were still negative on the 29th day. A further experiment in which half the above amount of each drug was given as before for a period of four days showed that sulphadiazine was effective at this dose whereas five out of 12 birds receiving sulphaguanidine showed parasites in their blood between the 11th and 18th day and two of them died as well as all the controls.

The drug levels attained in the blood by the above dosage were higher than those normally reached in human therapeutic experiments. The authors conclude that sulphadiazine exerted a definite prophylactic action under the conditions of the experiment while sulphaguanidine was less effective.

J. D. Fulton

BLACKWATER FEVER.

OLIVER-GONZÁLEZ J. Blood Agglutinins in Blackwater Fever *Proc Soc Exper Biol & Med* 1944 Oct v 57 No 1 25-6

Sera from two cases of blackwater fever were examined for the presence of α , β and cold agglutinins. Both sera contained α and β agglutinins which were absorbed. Sera were also treated with polysaccharide obtained from *Ascaris suum*. After absorption with A and B agglutinogens and the *Ascaris* polysaccharide both sera were found to contain cold agglutinins.

The author suggests that in blackwater fever auto-agglutination may result from immunization of the host with a substance in the malaria parasite related

to human isohaemagglutinogens. There is some evidence that the malaria parasite can behave in this manner since α and β agglutinins may be increased during the disease.

The possible relationship between the presence of cold agglutinins and the development of blackwater fever is discussed.

Cold agglutinins were not found in two specimens of sera from blackwater fever cases in West Africa tested in Britain.

B G Margraff

RIVERA LUGO I The Pathology of Blackwater Fever *Bol Asoc Med de Puerto Rico* 1944 Nov v 36 No 11 461-7 6 figs [8 refs]

TRYPANOSOMIASIS.

SAUNDERS G F T HOLDEN J R & HUGHES, M. H. Second Report on the Treatment of Trypanosomiasis by Pentamidine *Ann Trop Med & Parasit* 1944 Dec 30 v 38 Nos 3 & 4 159-68 1 chart.

In a previous paper this *Bulletin* 1942 v 39 532 the author reported on the treatment of 14 cases of Gambian sleeping sickness with pentamidine they comprised "early cases central nervous system cases unsuccessfully treated" cases previously treated with other drugs. In the present paper the results of a follow-up of some of these cases during one to three years are shown and notes on 12 new cases also treated with pentamidine are given. The condition before and after treatment with pentamidine of these and of other cases making a total of 50 is also shown in a table.

Pentamidine was given by intravenous injection in doses of from 0.05 to 2 mgm. per kgm. of body weight the course varying from 10 to 37 injections usually once a day but in some cases twice or three times a day. The only serious immediate effect of an injection was a fall of blood pressure which might be dangerous a chart shows observations of blood pressure taken at half-minute intervals after an injection and the effect of a preliminary injection of atropine which prevented the fall but was followed within a few minutes by an abnormal rise. If the injection was given very slowly however the fall was very slight.

The immediate clinical result was very good of eight earlier cases with a cell count under 30 per cmm. only one had relapsed of 16 cases with a cell count over 30 or with advanced symptoms 10 showed no improvement six improved but four relapsed within two years while two patients with over 600 cells were still in good health after over two years.

The author concludes that patients whose cerebrospinal fluid contains less than 30 cells per cmm are usually cured when the cell count is above 30 a relapse usually follows treatment and in very advanced cases the drug is useless.

EAGLE H A New Trypanocidal Agent V-(p-Arsenophenyl)-Butyric Acid *Science* 1945 Jan. 19 69-71

This new trypanocidal compound was found to be the most promising one of a series of phenylarsenoxides which were tested on *Trypanosoma equiperdum* in mice and rabbits [this *Bulletin* 1945 v 42, 15]. It is slightly soluble in water readily soluble in dilute alkali and neutral solutions of the sodium salt have withstood sterilization in the autoclave and have afterwards been kept in

sealed ampoules at room temperature for a year without demonstrable change. The chemotherapeutic index [this *Bulletin loc cit*] in mice and rabbits was higher than that of tryparsamide. Cultures of *Schizotrypanum cruzi* were killed within four hours by dilutions in excess of 1:400,000. The author has received personal communications from workers in other laboratories that this compound was found to be effective against *T. rhodesiense* in mice (C. M. SCOTT) and in *T. gambiense* infections in guinea pigs, chimpanzees and man (VAN HOOFF, HENRARD and PEEL). trypanosomes resistant to arsenicals were sensitive to this drug.

In the summer of 1944 it was tried in human trypanosomiasis by SAUNDERS in the Gold Coast, McLEITCH in Nigeria, FINDLAY in the British West African Forces and by VAN HOOFF in the Belgian Congo. It was supplied as a 2 per cent. solution in ampoules; the dose varied from 0.25 to 0.5 mgm. per kgm. of body weight (usually doses of 0.8 to 1.5 cc. of the solution were injected). It was given intravenously (sometimes intramuscularly, causing little pain) twice a week, three times a week, or daily; the total number of injections varying from 6 to 24. So far over 200 patients have been treated and the following conclusions have been drawn: (1) in 800 injections given in over 100 early cases no toxic reaction occurred except that about 2 per cent. of the injections produced nausea and vomiting; (2) trypanosomes disappear from the peripheral blood and lymph glands within 30 to 60 minutes after the first injection; (3) early cases can be cured within two weeks by daily injections of about 0.4 mgm. per kgm.; (4) it is ineffective in clinically late cases and may cause toxic encephalitis in such patients; (5) it gave good results in a few infected sheep and one horse but in a few cattle in which it was tried the trypanosomes persisted [species of trypanosome not stated]. There is therefore reason to think it may be useful in some but not all forms of animal trypanosomiasis.

J. F. Corson

BRAUSS F. W. Untersuchungen ueber die Wirksamkeit neuerer Chemotherapeutika gegenueber Nagana Trypanosomen. [The Activity of some New Drugs on Nagana Trypanosomes.] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1944 Mar 30 v 105 No 2 104-10.

These experiments were begun in 1939 and were interrupted by the war. Having found that various sulphonamide compounds had no action on *T. brucei* infections in mice, the author tested a guanidine derivative called Anticom and found that it failed to cure although it cleared the peripheral circulation of trypanosomes within 24 hours. Surfen was the next compound to be tried. *in vitro* it caused morphological changes in the trypanosomes similar to those produced by Germanin and the trypanosomes became immobile. Experiments *in vivo* showed that a 20 gm. mouse could tolerate 50 mgm. injected intraperitoneally; doses of 0.05-0.5 mgm. prolonged the life of the infected mouse while doses of 1-10 mgm. cured it but a dose of 0.5 mgm. given 24 hours after the infecting inoculation cured the mouse. If this dose was given later than 24 hours the mouse died although the peripheral blood remained free from trypanosomes.

Mice were protected by 1 mgm. given 48 hours before the infecting inoculation as the drug is quickly removed from the blood no prolonged protective action can be expected.

The trypanosomes of the relapse after a subcurative dose required a larger dose to cause their disappearance from the blood than before.

By giving subcurative doses and making subinoculations the trypanosomes became more resistant requiring 1/10 of the tolerated dose instead of 1/50 for cure in the case of untreated infections.

Surfen was also tried against *T. congolense* and *T. equiperdum* it was effective against *T. equiperdum* and ineffective against *T. congolense* but for the latter infection treatment with "Congasin Bayer" is successful. The author concludes that Surfen is a useful trypanocide but it is less effective than Germanin.

J. F. Corson

EAGLE H. & MAGKUBOS H. J. The Spontaneous Development of Arsenic-Resistance in *Trypanosoma equiperdum* and its Mechanism. *J. Pharm. & Exper. Therap.* 1944 Oct v 82 No. 2, 137-51 1 fig. [23 refs.]

A strain of *T. equiperdum* formerly sensitive to phenyl arsenoxides, was found by *in vitro* methods to have become markedly resistant to ammo- and amide-substituted derivatives of the parent substance in the absence of all drug treatment. The strain remained sensitive to the parent substance as well as to methyl chloro or acid-substituted derivatives. The resistance persisted during at least 30 passages in mice and 2 in rabbits. It was definitely established that the change was due to difference in susceptibility of the organisms and not to variation in the drugs used. The nature of arsenic resistance in trypanosomes has been discussed by YORKE *et al.* [this *Bulletin* 1933 v 30 447] and resembles that encountered in the present instance. Various theories have been put forward in explanation of resistance in prepared strains such as increased tolerance to the drugs or failure to combine with them. The present authors noted that the living trypanosomes no longer bound certain of the compounds to which they had become resistant but did bind those to which they were still susceptible as YORKE *et al.* [this *Bulletin* 1931 v 28, 910] had found in the case of a resistant strain of *T. rhodesiense*. HOGAN and EAGLE (*J. Pharm. & Exp. Therap.* 1944 v 80 93) have recently demonstrated that the widely varying toxicity of different arsenicals is related to the degree to which they are bound by the tissues. The theories on the mechanism of selective arsenic resistance are discussed. In inducing resistance in trypanosomes by repeated exposure to an arsenical, the authors suggest that the compound may simply act as a factor which allows a spontaneous variant to become apparent by killing off the more susceptible organisms. In this connection it is to be noted that resistance is not always specific for the compound producing it. The above theory does not explain however why the variant strain in the present instance having arisen spontaneously suppressed the parent strain. The view of spontaneous variation is however supported by the fact that resistance often becomes maximal soon after it first becomes apparent.

J. D. Fellow.

BURR E. D. A Note on Variation in Living *Glossina brevipalpis* Newstead (Diptera) with particular reference to a Red-Coloured Form found in Nature. *Proc. Roy. Entom. Soc. of London* Ser. A, Gen. Entom. 1944 Dec. 23, v 19 Pts 10-12, 137.

LEISHMANIASIS

KHODUKOV N. I. [Focal Distribution of Visceral Leishmaniasis in Tashkent for Twenty Years and the Problem of the Reservoir of Infection.] *Med. Parazit. & Parazit. Dis.* Moscow 1943 v 12 No. 6 61-9 [In Russian.]

The author records some of the results of observations on visceral leishmaniasis carried out in Tashkent (Central Asia) during the last 20 years. One of the most remarkable features of this disease is its focal distribution in the town most cases occurring in localized areas without a tendency to spread outside them. In

spite of the fact that sandflies are uniformly distributed throughout the endemic region. The restricted localization of this disease is attributed to the existence of reservoir hosts especially dogs the rôle of which in the spread of leishmaniasis has been suspected for a long time. The data in favour of this view are on the one hand aetiological and clinical, and on the other epidemiological. Thus the canine and human parasites (described as *Leishmania canis* and *L. infantum* respectively) are morphologically indistinguishable, have the same antigenic properties and are infective to the same laboratory animals. Moreover the course of the disease and the pathological changes are the same in children and in dogs and the areas of distribution of the disease in both hosts coincide. From the epidemiological point of view man is actually of secondary importance since the parasites are soon eliminated from the peripheral circulation whereas the dog constitutes a massive source of infection for sandflies because in the early stages of the disease the primary lesions are represented by extensive multiple papules situated on the muzzle while later the infection becomes generalized in the skin. In this connexion it should be taken into consideration that the rate of infection in sandflies depends largely on the abundance of parasites in the skin of the dog and that the spread of the infection from dog to man is facilitated by the close contact between the two since they usually share the same dwelling. From these observations it is concluded that the dog is the most important reservoir of infantile kala azar in Central Asia though there also appears to be some evidence of transmission from man to man and from man to dog. The rôle of the dog as the source of leishmanial infection is further enhanced by the occurrence in these animals of symptomless infections (in 5-9 per cent.) which may remain inapparent for periods exceeding six months. It is doubted if sandflies can serve as a reservoir for the examination of many thousands in the course of about 14 years revealed infected insects only in places where there was a concentration of infected dogs the insects thus serving merely as vectors. The possibility of rats, mice and lizards serving as reservoir hosts of leishmaniasis was also considered but the examination of these animals has so far failed to reveal the presence of leishmania. C. A. Hoare

MALONE R. H. & BROOKS A. G. Transmission of Kala Azar in India. The Case against the Sandfly. *Indian Med Gaz* 1944 Oct v 79 No 10 484-93 [44 refs].

In this paper the authors argue against the acceptance of the view that kala azar in India is transmitted by *Phlebotomus argentipes* and this in spite of the fact of successful transmission of the disease to all of five (not seven) volunteers by the bites of infected sandflies. They maintain that there is no real correlation between the distribution of kala azar and that of the sandfly, there being areas such as Ceylon where the sandfly occurs while the disease is absent. It is claimed that the whole system of breeding and maintaining sandflies in India for experimental purposes is quite unnatural and that it has resulted in the flies being kept alive longer than their natural span of life and that this combined with an artificial diet of raisins has produced the phenomenon of the blocked fly which has the anterior part of its alimentary tract crowded with flagellates. It is with these abnormal flies which have no counterpart in nature that transmission has been effected. Blocked flies have never been met with in the wild state and though naturally infected flies have been discovered their number is too small to support a claim that this fly is the vector.

It is held that *Leishmania donovani* is not a blood parasite but one of the reticulo-endothelial system and that it cannot therefore be regarded as similar to blood parasites which are transmitted by insects. Furthermore it is not remarkable that an organism should flagellate (not in the sense of flagellation of

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a malarial parasite) in an unnatural host. So the parasite of kala azar assumes its flagellate stage not only in the sandfly but also in the bed bug [and it might have been remarked also in the test tube]. As an illustration of the association of a parasite with an unnatural host the production in mice of a leishmania like infection by the flagellate of the water scorpion is mentioned [in spite of the fact that this claim has been completely disproved since it was first made]. Again kala azar in India is rarely seen before the age of two. It is commoner in the age period 6 to 20 and is about three times as common in males as in females. These limitations it is claimed cannot be reconciled with the sandfly hypothesis.

The authors state finally that sufficient attention has not been paid to the skin, which has been shown to be frequently infected with leishmania. Infections have sometimes spread from one experimental animal to another when living in contact and it is suggested that the possibilities of the spread of kala azar by way of the skin as a result of abrasions, pathological conditions arising from excessive sweating, lack of cleanliness be investigated. The authors write—

"We venture to suggest that the supporters of the sandfly theory of transmission have been carried away by the results of laboratory experiments, have not paid sufficient attention to the study of the fly in nature and have ignored or denied the mass of epidemiological evidence which casts grave doubt on the correctness of their theory."

As the Editor remarks in his note to the paper, this article outlines the many points about the transmission of kala azar in India which are still far from clear and of which further investigation is necessary. Nevertheless it is hardly a refutation of the sandfly theory which is receiving increasing support from countries outside India for both kala azar and oriental sore.

SEA GUPTA, P. C. The Value of the Complement Fixation Test in the Diagnosis of Kala-Azar. *Indian Med. Gaz.* 1944 Oct 19 No 10 483-9. C. M. Wrenyon

In an earlier publication the author gave an account of the results of a complement fixation test for kala azar in which an antigen devised by WITENSKY, KLINGENSTEIN and EISEN (WKE antigen) was used. This *Bulletin* 1944 v 41 17. Though it was prepared from tubercle bacilli it had a marked degree of specificity for kala azar. In the present paper a more extensive series of tests have been carried out with a WKE antigen prepared not from tubercle bacilli but from more easily cultivated acid fast organisms—*Mycobacterium phlei* and the so-called leprosy bacilli of Hedrowaki, Lleras, Bayon and Duval. Of 260 cases of kala azar 241 gave a positive reaction, 16 a doubtful reaction and three a negative reaction. Of 604 cases which might be considered in the differential diagnosis of kala azar 99 per cent gave a negative reaction. A positive reaction is obtained in a small proportion of obvious cases of chronic pulmonary tuberculosis. For the early diagnosis of kala azar the test is very useful, some cases giving a positive reaction within three weeks of the onset. The chances of obtaining a positive indication of kala azar are probably greater with this test than by sternal puncture.

C. M. Wrenyon

ARMITAGE, J. E. & BOLLIGER, A. Transmission of Kala-Azar to the Pouch Young of the Common Australian Possum (*Trichosurus vulpecula*) [Correspondence.] *Nature* 1945 Feb 3 145-6.

The authors infected a 2½ months old common opossum of Australia (*Trichosurus vulpecula*) with kala azar by infecting intraperitoneally 1 cc. of broth washings of a culture of kala azar on N.N.N. medium. The mother was

anaesthetized and the young animal which was still attached to the mother's nipple was lifted out of the pouch inoculated and replaced in the pouch. About a month later the young animal began to leave the pouch although eating and moving about. It was weak and underweight and had a distended abdomen owing to enlargement of the spleen and liver. At 10 weeks a heart puncture was made to obtain blood and the animal died a few minutes later. At autopsy the spleen weighed 8.9 gm. (five times the normal weight) the liver 26 gm., the left kidney 3.4 gm. and the right kidney 3.2 gm. The blood showed microcytic anaemia with a colour index of 0.69 and marked neutropenia (4 per cent). Leishman Donovan bodies were present in a smear of the spleen and in sections of liver and bone marrow in cultures from the blood, spleen and sternal marrow the flagellate form of the parasite was seen. The mother was killed three months afterwards and no evidence of infection was found post mortem.

J F Corson

SENEKJIE H A American Visceral Leishmaniasis—the Etiological Agent.
J Parasitology 1944 Oct v 30 No 5 303-8 1 fig [24 refs]

When in 1934 PENNA reported that the viscerotomy survey as carried out in Brazil for the purpose of identifying deaths from yellow fever had revealed the existence of kala azar it was supposed that this was a special type of the disease caused by a new species of *Leishmania* viz *L. chagasi*. Various arguments in support of this conclusion were advanced but all these have been shown to be unfounded. In the present paper the author reviews this situation and shows that the biochemical, cultural and growth requirements as well as the bile solubility and the thermal death point of the S American parasite are the same as those of *L. donovani*. He concludes as others have done that the name *L. chagasi* is a synonym of *L. donovani*.

C M Wenyon

KEAN B H Cutaneous Leishmaniasis on the Isthmus of Panama. Arch Dermat & Syph 1944 Oct v 50 No 4 237-8

In the forty year period (1904-1944) over 500 000 patients were admitted to the Gorgas Hospital Panama. Amongst these it has been possible to collect 15 cases of proved cutaneous leishmaniasis and of these 6 were diagnosed in the year 1943-1944. Most of the cases were in persons who had come to Panama from elsewhere and had resided there for at least seven months. In all cases the disease was acquired in the non-sanitated bush areas. The recognition of six infections in the last year is undoubtedly associated with the recent increase in military activities. Nine of the patients had single sores while six had multiple lesions. The mucous membranes of the naso-pharynx were involved in one case. The lesions were most unusually seen on the ear or on the dorsum of the forearm wrist or hand. A striking feature of several cases was a nodular lymphangitis in the areas draining the ulcers. Treatment with antimony potassium tartrate or foudadin was efficacious. The only previous records of cutaneous leishmaniasis in Panama are from case reports of over 30 years ago. In a note to the present paper it is reported that an endemic focus has been discovered in Arraijan, Panama.

C M Wenyon

BERBERIAN D A Cutaneous Leishmaniasis (Oriental Sore) II Incubation Period Arch Dermat & Syph 1944 Oct v 50 No 4 231-2 [10 refs]

In a previous paper [this Bulletin 1939 v 36 1035] the author reported that in 35 cases of oriental sore induced by the inoculation of suspensions of flagellates from cultures of *Leishmania tropica* the incubation period had varied from two

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weeks to six months. Other observers who have practised this protective inoculation have noted incubation periods of three weeks to 11 months two to 12 months two to eight weeks less than a fortnight to more than two months. In the author's experience the incubation period varies with the quantity of the inoculum the depth of the inoculation and the individual susceptibility. Occasionally the incubation period is prolonged. To illustrate this three cases are reported. In all three culture flagellates were inoculated intracutaneously on the left thigh the lesions being first noted after 18, 30 and 56 months respectively. (For part I of this series see this *Bulletin* 1945 \ 42 102.)

C. M. Wenyon

BERNERLY D. A. Cutaneous Leishmaniasis (Oriental Sore) III. Period of Infectivity of Saline Suspensions of *Leishmania tropica* Cultures kept at Room Temperature. *Arch. Dermat. & Syph.* 1944 Oct. v 50 No. 4 233

Leptomacids from cultures of *Leishmania tropica* grown on modified N.N.N. medium and suspended in isotonic solution of sodium chloride will remain alive for seventeen days at laboratory temperatures varying from 15.8 to 38.3°C. The suspension which was distributed in 0.5 cc. amounts in ampoules contained approximately 3,350,000 leptomacids per cc. Viability was proved by the production of oriental sore in volunteers (intracutaneous inoculation of 0.1 and 0.2 cc.) and the presence of motile flagellates. The observations were made to meet the need of physicians in districts distant from laboratories who require suspensions for purposes of immunisation.

C. M. Wenyon

BERNERLY D. A. Cutaneous Leishmaniasis (Oriental Sore) IV Vaccination against Oriental Sore with Suspensions of Killed *Leishmania tropica*. *Arch. Dermat. & Syph.* 1944 Oct. v 50 No. 4 234-6. (Refs. in footnotes.)

The author who has done a considerable amount of work on the subject of immunity in oriental sore has shown that sores may be induced, for the purpose of producing immunity, by the intracutaneous inoculation of suspensions (in isotonic saline solutions) of the flagellate form of *Leishmania tropica*. As in the naturally acquired disease immunity does not develop till the sores are commencing to heal but as has long been known, the immunity when acquired is permanent. The author has also attempted to produce immunity in two volunteers by the inoculation of flagellates which had been killed by suspending them in 0.5 per cent phenol in saline. The results were entirely negative but in view of the successes reported by PERROA and PESTANA [this *Bulletin* 1942, v 39 674] in S. America the author is led to record his experiments here. Of the 32 volunteers 9 received one, 8 two and 15 three injections of the killed vaccine. At intervals varying from 31 to 337 days after vaccination the volunteers together with unvaccinated controls and others who had recovered from oriental sore were inoculated with suspensions of living flagellates. The only persons who did not acquire oriental sore were those who had recovered. It is thus clear that the vaccination with killed flagellates did not produce any immunity. The author finds it difficult to account for the successes reported in S. America where however no attempt was made to test the immunity of vaccinated persons by experimental inoculations. He considers the four-month period of observation too short. It should have been extended to a number of years. It seems clear that the S. American work needs confirmation.

C. M. Wenyon.

KATZENELLENBOGEN I Vaccination against Oriental Sore. Report of Results of Five Hundred and Fifty-Five Inoculations. *Arch Dermat & Syph* 1944 Oct v 50 No 4 239-42 1 fig

At the Palestine Potash Plant at the northern end of the Dead Sea, where oriental sore has become hyperendemic, the author vaccinated 556 persons with living leishmania from cultures or the spleens of infected hamsters. It was possible to follow up 416 of these and it was found that a vaccination sore developed in 237 after an incubation period varying from less than a fortnight to 18 months. Of those vaccinated 11 were children the youngest being three months old. The course in children was the same as in adults except in one case where as a result of trauma there developed a slow-healing flat ulceration of the size of the child's palm and resembling scrofuloderma. Healing occurred in three months. When a sore is developing there appears at the end of the incubation a bluish red papule which persists for three to six months. The papules are easily injured, and may thus be converted into ulcers. There does not seem to be any reason to record the sores as nodules or ulcers.

In 45 cases a reaction occurred after vaccination. There was swelling at the site of injection sometimes with infiltration of an area the size of a palm. Temperature up to 103°F might be noted with local pain and tenderness of the inguinal lymph nodes. The condition lasted not more than one to three days. In only four of these 45 did a vaccination sore develop. It would seem that the reaction was allergic in nature for 26 of the subjects had resided in the area for several years. Such reactions are known to follow vaccination in persons previously infected with leishmania. On the other hand 27 persons who had been living in the area for several years and who showed no obvious signs of healed sores failed to develop sores on vaccination. Seven of these were vaccinated on two subsequent occasions also without result. In these the possibility of a natural immunity has to be considered.

Persons inoculated six to eight months after the appearance of natural sores may develop at the site of inoculation nodules which contain no leishmania and which disappear within a few days or a week. Such reaction nodules may follow the inoculation of persons who have been suffering from relapsing oriental sore of several years duration. The author's campaign of vaccination has had very favourable results. Thus at one settlement during the last two years there have been 95 new arrivals. Of these 25 were vaccinated on the thigh. Not one acquired a natural infection but of the 70 who were not vaccinated 65 became infected.

C M Wenyon

BELTRÁN E Acción de los cambios de pH sobre *Leishmania brasiliensis* en cultivo y sus contaminaciones bacterianas [Effect of Changes of pH of *L. brasiliensis* Cultures and their Bacterial Contaminations] *Rev Inst. Salubridad y Enfermedades Trop* Mexico 1944 June v 5 No 2 97-100 English summary

It occurred to the author who had cultivated *Leishmania brasiliensis* in N.N.N. medium with a pH of 7.2 that it might be possible to find a pH which would be favourable to the growth of leishmania and at the same time prohibit the growth of bacteria liable to contaminate the cultures. After trial of various pH under 7.2 it was found impossible to exclude bacterial growth without at the same time excluding the leishmania.

C M Wenyon

FEVERS OF THE TYPHUS GROUP

GEAR, J. The Rickettsial Diseases in South Africa with special reference to
Louse-borne Typhus Fever. *Proc Transvaal Med Officers' Ass* 1944
Aug v 24 No 283 23-34 3 charts Discussion 34-7

The following points of general interest are taken from this concise and vivid account of louse-borne typhus in South Africa.

The classification of the typhus fevers proposed by FELIX [this *Bulletin* 1943 v 40 230], and based on the agglutination responses has the advantage that these reactions can usually be determined, but in many cases they do not indicate the vector concerned and this from the point of view of the Health Officer is the most important consideration. The classification proposed by MEGAW [this *Bulletin* 1931 v 28 (23)] based on the vector has the disadvantage that in any one case the vector is very rarely seen but a consideration of the attendant circumstances usually though not always gives a clear clue to its identity and at present this classification into louse typhus, flea typhus, tick typhus and mite typhus is considered to be the most valuable.

In South Africa mite typhus is unknown, the other three types are of widespread occurrence.

The differentiation of louse typhus from flea typhus on epidemiological grounds is often difficult because of the frequent coexistence of infestation by lice and rats. Tick typhus is usually easy to diagnose in South Africa. In most cases it is acquired by persons picnicking or camping in rural areas though sometimes infection is associated with the presence of tick-infested dogs in the homes. There is usually a characteristic local lesion the rash is papular and when profuse it extends to the face palms and soles.

The Weil-Felix test, although non-specific is one of the most reliable of the laboratory methods of diagnosis. It does not differentiate louse typhus from murine typhus and sometimes does not differentiate these from tick typhus. In tick typhus *Proteus* OX19 and OX2 are agglutinated on the average at about equal titres and OXK is often agglutinated as a rule at a lower titre. In most cases the agglutins appear later than in louse-typhus—about the 10th day. When OX3 alone is agglutinated the case is almost certainly one of tick borne typhus.

A more specific reaction is the one based on the agglutination of the can rickettsiae but even this sometimes fails to differentiate louse typhus from tick typhus. It usually gives a clear-cut differentiation of tick typhus.

A monocytosis of 7-15 per cent. is a constant and characteristic feature of typhus fever. Although flea typhus is widespread in South Africa relative few cases have been reported. Contrary to previous reports the Weil-Felix titres in louse typhus in South Africa are just as high as in Europe. In three consecutive cases the titres were 1-1,000 1-2,800 and 1-25,000.

John W. D. Meyer

GREIFF D. PICKERTON H. & MORAGLES V. Effect of Enzyme Inhibitors and Activators on the Multiplication of Typhus Rickettsiae. I. Penicillin, Para-Aminobenzoic Acid, Sodium Fluoride, and Vitamins of the B Group. *J Exper Med* 1944 Dec 1 v 80 No 6 561-74 1 fig [14 refs.]

The effects of penicillin para-aminobenzoic acid (PABA) sodium fluoride and vitamins of the B group on the growth of murine rickettsiae in yolk-sac cultures were tested by the authors. The ingenious technique adopted will be of interest to other workers on the same lines.

The authors have already reported the action of penicillin in inhibiting rickettsial growth in yolk-sac cultures and the beneficial effect of the drug

when given early to mice infected with typhus fever [this *Bulletin* 1944 v 41 839 and 840] UNGAR (*Nature* 1943 v 152 245) [*Bulletin of War Med* 1944 v 4 301] has reported that PABA enhances the bacteriostatic effect of penicillin on some microorganisms

In the present experiments the authors found that PABA injected in doses of 3.3 mgm. into infected yolk sacs had an inhibiting effect equal to that of 1 000 units of penicillin. Meta aminobenzoic acid and ortho-aminobenzoic acid had no demonstrable effect.

PABA was added to the food of 23 dba mice infected with murine typhus [The dba (dilute brown) strain of mice has been developed from a single pair by Dr C. C. LITTLE and has been inbred, for the most part by brother to sister matings since 1909] The drug was given from the first day after inoculation and in a strength of 3.0 per cent. Only one of the mice died of typhus another died of some other disease on the 4th day All the 23 untreated control mice which had been infected in the same way died of typhus fever on the 6th or 7th day

Sodium fluoride accelerated the rate of growth of the rickettsiae in yolk-sac cultures Various vitamins of the B group had no effect on the growth of the rickettsiae

The favourable therapeutic effects of para-aminobenzoic acid in human typhus fever [this *Bulletin* 1945 v 42 201] reported by YEOMANS *et al* were not known by the authors when they were engaged on the present experiments

John W. D. Megaw

NELSON J. H. & CRICKSHANK J. C. Agglutinins to *Proteus* OX19 in the Serum of Pregnant Women. *Monthly Bull. Ministry of Health & Emergency Pub Health Lab Service* (directed by Med Res Council) 1945 Jan. v 4 19-25 1 chart.

The authors have not been able to confirm the finding reported by GRACE that the sera of pregnant women agglutinate *Proteus* OX19 constantly and at high titres [this *Bulletin* 1944 v 41 197] They have found that when an Oxford Standard Suspension of *Proteus* OX19 was used 6-10 per cent. of the sera of pregnant women agglutinated the organism at a titre of 1-100 or over The two authors worked independently of each other and the following table shows their findings —

Number of sera	Percentage agglutinating <i>Pr. OX19</i> at or over these titres (Ipswich series by J. H. N.)				
	1-20	1-40	1-80	1-160	1-320
Normal sera 33	39.4	24.2	12.1	3.0	0
Pregnancy sera 132	87.1	62.1	33.4	10.6	0.8
(Exeter series by J. C. C.)					
	1-16	1-32	1-64	1-128	1-256
Normal sera 20	35	20	5	0	0
Pregnancy sera 50	88	64	32	6	2

In the Ipswich series an attempt was made to determine the stage of pregnancy at which agglutination responses were most frequent No special trend could be detected but among 50 sera taken during the 5th and 6th months 76 per cent. reacted at 1-40 44 per cent. at 1-80 and 16 per cent. at 1-160

Other organisms were found to be agglutinated more frequently by the sera of pregnant women than by normal sera CRICKSHANK found the following

percentages of reactions at titres of 1-80 or over among 45 pregnant women. *Proteus* OX2 8.3 *Bact typhosum* O 4.4 *Bact paratyphosum* BO 13.3. Sera of 27 pregnant women did not agglutinate suspensions of epidemic and murine rickettsiae although the sera used had already agglutinated *Pr* OX19 at titres of 1-40 or over.

The authors state that in the absence of more detailed information concerning technique they are unable to explain the difference between their findings and those of Gratch. They suggest that he may have used a hypersensitive strain and they point out that no mention is made of the use of a standardized suspension. They do not exclude the possibility that Gratch's strain possessed some distinctive character but they conclude that the test is not likely to have any application in the early diagnosis of pregnancy.

The difference in the findings seems to be best explained by the existence of a "distinctive character" in Gratch's strain. A happy event of this kind would not be unprecedented, because according to FELIX, *Proteus* OXK is an antigenic variant of *Pr* OX19 being derived from a culture of that organism supplied by the National Collection of Type Cultures. It is to be hoped that the "Gratch strain" is still available and that subcultures will be found to be as "specific" for the sera of pregnant women as *Pr* OXK is for the sera of mite-typus patients. *John W. D. Meigs*

VARELA, G. Presencia en el cobayo normal de un antígeno que origina la reacción de Weil-Felix. [The Presence in the Normal Guinea-pig of an Antigen which gives rise to the Weil-Felix Reaction.] *Rev Inst Salubridad y Enfermedades Trop. Mexico*. 1944 Sept., v 5 No. 3 191-3. English summary (4 lines).

Suspensions prepared by triturating the lungs of healthy guinea-pigs in normal saline were injected intravenously on six occasions into each of two healthy goats whose sera had been found to contain no agglutinins for *Proteus* X19 or *Pr* XK. A week after the last of these injections the sera of the goats agglutinated both of the above organisms at a titre of 1-160. By absorption and precipitation tests the agglutinins in the goats' sera were found to behave in the same way as one contained in the sera of typhus patients.

The author believes that "the absence of the Weil-Felix reaction in typhus-infected guinea-pigs is due to the presence of this antigen." He considers that the antigen which the guinea-pig possesses in common with the *Proteus* organisms is contained in the endothelial cells of the animal, and that this distribution accounts for the fact that the lung is specially rich in the antigen.

John W. D. Meigs

STEVENS, R. S. Louse-borne Typhus Fever. Trial of Serum Treatment. *Lancet*. 1945 Jan. 27 103-9 10 charts.

Hyperimmune rabbit serum made by the Lederle Laboratories was tried by the author in the treatment of seven cases of louse-borne typhus at a hospital in the Middle East. In the first case doses of 40 cc. were given intravenously on the 6th and 7th days but the patient died on the 9th day. He belonged to the 36-39 age group. In the other six cases the treatment was started as soon as the diagnosis was made. The dosage was 40 cc. intravenously and 40 cc. intramuscularly on the first day of treatment, 40 cc. intramuscularly on the next day, and 20 cc. by the same route on the following days till necessary for the treatment was no longer apparent. All these patients survived, and there were grounds for believing that their condition had been improved by the injection of serum, though the author states that "no attempt is made to draw conclusions from so small a series."

Among 14 patients who had been treated in the hospital before the serum became available there were five deaths. Brief notes are given of the 21 cases. It is mentioned that the average delay in appearance of a Weil Felix titre of 1-100 was 11.6 days. Two patients who died had completely negative reactions on the 8th day, and in another fatal case the titre was 1-40 on the 7th and 11th days. Rickettsiae were isolated from two of these three patients. Rickettsia agglutination reactions were positive at high titres in the six cases in which the test was carried out.

John W. D. Megaw

LAMPERT H. Eine neue Allgemeinbehandlung schwerer Infektionskrankheiten erläutert am Fleckfieber [A New General Method of Treatment of Severe Infectious Diseases, as Applied to Typhus Fever] *Munch med Woch* 1944 May 5 v 91 No 17/18 223-5

The author has already claimed that he has obtained excellent results in the treatment of typhus fever by the daily use of warm baths, daily intravenous injections of artificial blood, and repeated subcutaneous or intravenous injections of saline solutions [see this *Bulletin* 1942 v 39 824 and 1943 v 40 831]. Further evidence in support of this claim is now produced, but as was the case in connexion with the previous papers it is not easy to assess the significance of the results that have been reported.

In the first set of figures the controls consisted of patients in a neighbouring hospital. In January and February 1942 there were no deaths among 104 patients treated at the author's hospital, and at the other hospital the fatality rate was 13.3 per cent. In the following two months 11 per cent of the author's patients died, and 14.4 per cent. of the controls.

The physician whose patients served as controls in the above series later applied the hot-bath treatment to 96 of his patients, and 10 of these died, whereas the fatality rate for all the 323 patients treated at the hospital during the same period was 13 per cent. No mention is made of the manner in which the 96 patients were selected for the treatment.

In November 1942 alternate patients were admitted to each of two hospitals of 100 beds. At one of these the combined treatment was carried out and the fatality rate was 6.7 per cent among 178 patients; at the other hospital no baths were given and intravenous injections were administered only in special conditions; the fatality rate in 185 patients was 17.8 per cent.

The author claims that his system of treatment has been demonstrated to be strikingly effective and he holds that it would be equally suitable for all severe infectious diseases.

The only information regarding the hot bath technique is contained in the statement that the bath at first ought to be at the same temperature as the patient and should be warmed gradually.

[It does not appear that the treatment has been adopted by other German physicians to the extent that would be expected if results comparable with those mentioned in the last of the above trials could be obtained by other observers.]

John W. D. Megaw

SERGEANT E. & HORRENBARGER R. Utilisation de la chèvre pour la préparation du vaccin non vivant contre le typhus exanthématique avec du virus provenant de pneumonie rickettsienne provoquée [The Use of the Goat for the Preparation of Killed Typhus Vaccine] *Arch Inst Pasteur d'Algérie* 1944 Mar v 22 No 1 8-10

The authors trace the history of the discovery by CASTAÑEDA [this *Bulletin* 1940 v 37 261] and by DURAND and SPARROW [*ibid* 1940 v 37 572] (independently) that the lungs of mice infected intranasally with rickettsiae

formed an excellent source of vaccine. Formalin vaccines prepared in North Africa were found to be effective and later the use of rabbit lung preparations was adopted by means of which the yield of vaccine was greatly increased. COMBESCU *et al* [*ibid.*, 1943, v 40 34] experimented with dogs but the yield was poorer in rickettsiae than that from mice but HORREXBERGER and RENOUX [*ibid.* 1945 v 42, 107] in Algiers found that sheep gave good results. It is now known that the yield from goats is as good as that from mice and the goat offers certain advantages over the other animals. It can be infected from the mouse.

The authors refer briefly to the protection given to those who work in the typhus laboratories—vaccination and regular re-vaccination, the use of protective clothing and masks, supplementary rations, adequate holidays and rest. In two years only three of 30 persons have contracted typhus which was slight. Thus by the standards in other laboratories is a low figure.

Charles Wilcocks

GIROUD P. Le tissu pulmonaire privé de Rickettsies par lavage et centrifugation possède un pouvoir antigène certain. [Pulmonary Tissue deprived of Rickettsiae by Washing and Centrifugation possesses Antigenic Properties.] *C. R. Soc. Biol.* 1943 May v 137 No 9/10 271-2.

The lung tissues of infected mice and rabbits were washed and centrifuged 13 times so as to separate as far as possible, the rickettsiae from the tissues. Rickettsiae could not be demonstrated in smears from this tissue but by enrichment methods the presence of small numbers could be confirmed. Vaccines were prepared in formal saline from the tissues thus largely (but not completely) deprived of the organisms, and were used for immunization tests, control animals being inoculated with the same vaccine but with the addition of the rickettsial suspension which resulted from the centrifugations.

The tissue vaccine gave protection similar to that afforded by the mixed vaccine to animals subsequently inoculated with a highly virulent strain of North African typhus. Lung tissue therefore in which there has been abundant growth of rickettsiae possesses good antigenic properties. Charles Wilcocks.

GIROUD P. Pouvoir pathogène et antigène sur cobaye de doses massives de Rickettsies du typhus historique conservées à -25° pendant des temps très longs. [Pathogenic and Antigenic Power of Massive Doses of Rickettsiae *provaschii* preserved at -25° C. for Long Periods.] *C. R. Soc. Biol.* 1943 May v 137 No 9/10 273-4.

Infected animal lungs were kept for 5 to 39 months at -25° C. in unsealed tubes, the tissues gradually dried. Doses corresponding to one-half or the whole of one lung were injected intraperitoneally into guinea-pigs at various times. The results were rather irregular but infection took place even with material preserved for more than 14 months.

Only those animals were found to be immune which had showed feeble evidence of infection. The author concludes, therefore, that the infective and antigenic powers of the rickettsiae are lost at the same time. It is improbable that attenuation with preservation of antigenicity can be achieved by these means.

Charles Wilcocks.

RUIZ MORENO, F. Caso de tifo exantemático en Baja California. [A Case of Typhus in Lower California.] *Medicina, Mexico*. 1944 Dec. 25, v 24 No. 474 471-2.

SINDEK H Zur Kreislaufpathologie des Fleckfiebers. [The Pathology of the Circulatory System in Typhus.] *Wien klin Woch* 1944 June 16 v 57 No. 23/24 298-301

COOK C E Observations on the Epidemiology of Scrub Typhus *Med J Australia* 1944 Nov 18 v 2 No 21 539-43 [12 refs.]

Three outbreaks of scrub typhus are discussed from the point of view of epidemiology.

Outbreak A consisted of 45 cases which occurred within a period of four weeks. Infection was confined to soldiers who had entered a strictly limited locality on the bank of a creek close to the edge of a jungle area. Although three divisions had been operating in the surrounding area of thickly wooded country and although scrub itch due to the bites of mites was very prevalent in the whole region no other cases of scrub typhus occurred.

Outbreak B also affected persons camping close to a creek in open forest country. There were 37 cases within a period of three weeks. No scrub itch occurred and mite surveys were unproductive.

Outbreak C In two brigade groups there were some hundreds of cases all from units camped near jungle fringes on the banks of streams. Units in the open valley for the most part escaped scrub typhus.

Infection was intense in very restricted foci limited to areas on the banks of jungle-clad streams and there was evidence that infection persisted year after year in certain foci. The incubation period ranged from 10 to 21 days.

A study of these outbreaks and of the available evidence on the subject of transmission led the author to doubt whether mites were really the vectors and he argues at some length that larval ticks are more likely to be responsible for transmitting the disease.

[This view is likely to give rise to sharp controversy so it is considered better to postpone a review of the arguments brought forward till the other side of the case has been stated.]

The author's view in brief is that there is no evidence to incriminate any one particular species of mite and that the epidemiology of the disease is consistent with its transmission by larval ticks.

[In the meantime preventive measures directed against bites by mites will be equally effective against tick bite and both of these arthropods must always be regarded as potential menaces to the efficiency of armies in the East.]

John W D Megaw

[The suggestions that scrub typhus may be transmitted by ticks has been made before by investigators in the Netherlands East Indies see KOUWENAAR and WOLFF this *Bulletin* 1936 v 39 442 and VAN DER SCHROEFF *ibid* 1941 v 38 684—Ed]

WILLIAMS R. W A Check List of the Mite Vectors and Animal Reservoirs of Tsutsugamushi Disease. *Amer J Trop Med* 1944 Nov v 24 No 6 355-7 [20 refs.]

The geographical distribution mite vectors and animal reservoirs of mite-borne typhus are shown in Table I. The author refers to the report of VAN DER SCHROEFF [this *Bulletin* 1941 v 43 684] on typhus in Northern Sumatra where ticks (*Amblyomma*) were possible vectors as well as mites and to a report by the U.S. American Typhus Commission [*ibid* 1944 v 41 841] on typhus in New Guinea where scrub itch and scrub typhus showed little correlation

TABLE 1
Mite vectors and reservoir animals of Tsutsugamushi disease

Geographical Distribution	Mite Vector	Reservoir
Australia	<i>Trombicula deliensis</i> Walsh, 1923 (1) <i>T. minor</i> (Kirsti-Sambon, 1927) (1) + <i>Laelaps australiensis</i> (2)	<i>Isodon torosus</i> - Bandicoot (1) * <i>Melomys fuscus</i> - Rat (1) * <i>Rattus assamensis</i> - Rat <i>Rattus conatus</i> * <i>Rattus norvegicus</i> (white strain) (1) * <i>Rattus norvegicus</i> (black and white strain) (1) * <i>Rattus rattus</i> (1)
China	<i>T. akamushi</i> Brumpt, 1910 (3)	
Formosa	<i>T. akamushi</i> (3, 4)	<i>Rattus rattus rufescens</i> (3, 9) <i>Rattus rattus rattus</i> (5) * <i>Rattus losea</i> (5, 11) <i>Rattus (Apodemus) agrarius</i> (5, 5) <i>Rattus norvegicus</i> (3) <i>Rattus musculus</i> (3) <i>Pachyura myrtae</i> - Mask Shrew (3)
India	<i>T. deliensis</i> (6) <i>T. akamushi</i> (6) <i>T. akamushi</i> (6)	<i>Mus (Rattus) rattus</i> (6) <i>Mus decumanus</i> <i>Mus berytus</i> (6) <i>Colunda allioti</i> - Indian brush (6) <i>Neotoma bengalensis</i> - Mole rat (6)
20	<i>T. akamushi</i> (4, 7, 9)	<i>Microtus monstrelli</i> Vole - (4, 7, 1) <i>Arvicola kishinouyei</i> - Field mouse (8)
21	<i>T. akamushi</i> (4) <i>T. deliensis</i> (9) ‡ <i>Schöps pasha höffners</i> Walsh, 1923 (9)	<i>Mus ethiops</i> (4) <i>Mus concolor</i> (4)
New Guinea	§ <i>T. minor</i> (10) <i>T. deliensis</i> (1)	<i>Echymipera cockerelli</i> - Bandicoot (10)
Palacadores Is.	<i>T. akamushi</i> (11)	<i>Mus rattus rufescens</i> (11)
Sumatra	<i>T. akamushi</i> (12) <i>T. deliensis</i> (9, 3) <i>S. schöffners</i> (9, 3)	<i>Rattus attus diardii</i> (9, 3) <i>Mus concolor</i> (3)

Animals in which the rickettsial organism has been demonstrated in nature, and which act as hosts of the mite vectors.

† Not a chigger mite.

‡ Thought to transmit the disease only from man to man. Belongs to genus *Neoschöngastia* as placed by some authors.

§ Some authors have placed the New Guinea form of this mite in the genus *Neoschöngastia*.

McCULLOCH R. N. Notes on the Habits and Distribution of Trombiculid Mites in Queensland and New Guinea. *Med J Australia* 1944 Nov 18 v 2 No 21 543-5

Medical entomologists must read this paper in its complete form but a few points of special interest to medical men in the East are given in the following abstract

The six-legged larval mites which attack man have much the same feeding habits as ticks they remain attached till fully engorged in some species this process takes as long as two days. Mites that are seeking a blood meal can safely be collected by a person whose clothes are impregnated with one of the suitable insecticides. The mites are picked up with a camel-hair brush moistened with alcohol as they travel across the boots of the collector who must stand quite still.

In West Queensland scrub itch is caused by *Trombicula minor* which may be exceedingly plentiful.

Mites are most active on warm days (67-75 F) and are inactive at temperatures below 60 F. They are not felt as they crawl over the skin or when biting or for 10-18 hours after attaching themselves. Then itching begins and the mites can be found in the centre of small raised and reddened areas of skin of about one-quarter inch in diameter.

In New Guinea the ankles were more heavily attacked than the trunk but on the Atherton Tableland in North Queensland the mites were on the parts of the body covered by clothing and not specially on the ankles.

It is suggested that the mites are attracted by sweat and so tend to travel till they reach a part of the body that is bathed in sweat.

There is no certain knowledge of the species of mites that are responsible for transmitting scrub typhus all of them must be suspected.

The author does not accept the suggestion that there is a special typhus mite which does not cause itch and which prefers to attack the trunk rather than the legs. He often found it quite impossible to predict that a given area of ground would be infested sometimes the mites are most numerous on grassy hills sometimes in the jungle. They are much more active after rain than during rain or in dry weather. They rarely climb higher than three inches up the stems of grass or bushes. Persons walking in infested areas are not likely to be bitten but standing still sitting or lying down whether by day or by night are direct invitations to the mites.

Cutting and burning the grass of camp sites reduces the number of the mites but does not eliminate them. Paths trampled ground, and the floors of tents or buildings soon become free from mites.

John W D Megaw

WILLIAMS S W SINCLAIR, A J M. & JACKSON A. V. Mite-borne (Scrub) Typhus in Papua and the Mandated Territory of New Guinea. Report of 626 Cases. *Med J Australia* 1944 Nov 18 v 2 No 21 525-39 11 figs (1 on coloured pl.)

This detailed account of the clinical features of scrub typhus is based on experience of 626 cases treated at an Australian general hospital in New Guinea between September 1942 and the end of September 1943. More than half of the infections were contracted during the fighting on the Moresby Buna trail 97 occurred during the campaign in and round Wau.

In most respects the description of the signs and symptoms corresponds closely with one of louse-borne typhus but some of the special features deserve attention.

By the end of the second week *Proteus O* YA was agglutinated at a significant titre in most of the cases. After attacks of average severity the patients became

[May 1945]

fit for duty at the end of 12 weeks after mild attacks this period was reduced to 6-8 weeks. Ambulatory attacks also occurred in which the only evidence of illness was the agglutination response.

There was some difficulty in getting a satisfactory strain of OAK but when this was secured, it was subcultured without loss of its agglutinability over a period of 12 months.

The rise in titre began between the 8th and 13th days the maximum was reached between the 14th and 22nd days. A significant titre was regarded as one showing a "two-tube increase" for example from 1-25 to 1-125 or from 1-50 to 1-250. When patients were seen for the first time late in the illness a titre of 1-125 was regarded as significant. Among 2,000 control sera, only one false positive was detected.

In 8 per cent. of undoubted cases the titre did not exceed 1-25 and in an additional 6 per cent. it was 1-50. Among fatal cases negative or non-significant reactions occurred in 25 per cent. of the patients though very high titres were observed in some.

A simple slide test was tried in 300 cases. One drop of serum previously diluted 1-4 was mixed on a slide with a drop of concentrated O.A.A. suspension, and the reading was made after rocking the slide for 2-3 minutes. The method was quite satisfactory with sera giving reactions of 1-500 or over with the standard method, but sera of lower agglutinability gave irregular reactions.

An analysis was made of the duration of the fever in 508 cases it was 4-8 days in 12 and 28-40 days in 15. The usual duration was 12-20 days. In 276 cases it ranged between 14 and 18 days.

An eschar was seen in 59 per cent. of the cases the patients seldom knew of its existence or of the bite that presumably was its cause. At the onset of the fever it was a rounded sore 2-5 mm in diameter surrounded by a dusky red raised areola, 3-4 mm in width.

The necrotic centre had sloughed out by the 10th to the 20th day leaving a punched-out ulcer surrounded by a bright-red areola. In rare cases there were two or more eschars in one case there were six. The site was seldom distal to the knee or elbow none occurred on the hand or foot.

A rash was seen in 65 per cent. of the cases it usually appeared between the fifth and eighth days at first there were reddish macules about 2-5 mm. in diameter on the chest and the front of the abdomen soon the spots became maculo-papular and the spots became larger.

Generalized enlargement of the lymph glands was observed in 68 per cent. of the cases it was pronounced by the fourth or fifth day and was usually greater in the glands draining the area of the eschar.

The leucocyte count was very variable during the first ten days the total count ranged from 3,100 to 12,400 per cmm. and during the second ten-day period it was 3,100-20,000 per cmm. The only significant change was in the lymphocytes whose numbers rose steadily in all the cases in which there was a good reaction to the infection, so that by the 8th to the 15th day counts of 3,000 were usual. In fatal attacks this increase in the lymphocyte count was exceptional.

The total fatality rate was 9.7 per cent. but there were remarkable variations: among the first 100 patients there was only one death among the second 100 there were two in the next 150 there were 37 (25 per cent.). The excessive mortality rate in the last-mentioned group was due to lowered resistance caused by great hardship dysentery and malaria. In the later period the fatality rate was 7.2 per cent.

The treatment was on the lines suitable for louse borne typhus the patients were nursed, when possible in the Fowler position a fluid intake of at least

140 oz. daily was aimed at the diet was well supplied with carbohydrates and proteins. Blood transfusion was very seldom needed except for a few cases of anaemia which occurred during convalescence. Cardiac stimulants were found to be of very little value. There was no evidence of permanent cardiac disability.

A typical eschar is well shown in a coloured photograph in the paper.

[This article is of exceptional value and importance at the present time it must be consulted by everyone who undertakes the work of describing the clinical aspects of mite-borne typhus as a war disease.] *John W D Megaw*

McDONALD S F Scrub Typhus. [Correspondence] *Med J Australia* 1944 Dec. 2, v 2 No 23 601

The author as a consultant and repatriation doctor calls attention to two points which he thinks were not emphasized sufficiently in the paper on mite-borne typhus by WILLIAMS SINCLAIR and JACKSON [above] they relate to the heart manifestations and the paralyses. Mite typhus as Williams *et al* stated leaves no permanent cardiac damage but a belief is common among both medical men and soldiers that any extra exertion during convalescence may cause sudden fatal heart failure. Such a view is very likely to produce many cases of D.A.H. The paralysis of the limbs also seems to clear up completely but sometimes it continues as a purely hysterical condition if it persists for more than a few weeks the muscles should be tested with the faradic current.

J F Corson

LIPMAN B L CASEY A V BYRON R A & EVANS E C Scrub Typhus. Results of a Study of the Cases of Two Hundred Patients admitted to and treated at a Station Hospital between Feb. 9 1943 and Feb 4, 1944 *War Medicine* Chicago 1944 Nov v 6 No 5 304-15 4 charts

This informative paper deals with the clinical features of scrub typhus of which 200 cases were seen by the authors at a hospital in North New Guinea between February 9th 1943 and February 4th 1944.

The patients were engaged in military operations in coastal and foothill areas.

A detailed account is given of the post mortem changes observed in six cases but in five of these lobar pneumonia had occurred as a complication so that as usually happens in the typhus fevers the picture was somewhat confused. The lesions uniformly present were the eschar lymphadenopathy the rash and enlargement of the spleen. In three cases the vessels of the pia mater were moderately injected. Small haemorrhages under the pleura in the pericardium and in the gastro-intestinal mucosa, were seen in two cases. The microscopic changes characteristic of the disease were the typhus nodules which were most conspicuous in the smaller vessels of the heart lungs and brain.

The incubation period was 9-14 days the eschar which was detected in 80 per cent. of the cases was usually formed during this period its presence had seldom been detected by the patient it was located on the extremities and trunk usually below the umbilicus. Regional or generalized lymphadenitis occurred in 98 per cent of the cases the femoral and inguinal glands were most often affected.

The prodromal period lasted 1-5 days and the chief features during this stage were malaise, headache backache pains in the orbital region and swollen and tender glands in the region draining the site of the eschar. The temperature was 99.6-102°F towards the end of the prodromal period. The onset was usually gradual though sometimes it was acute. The febrile period lasted 14-18 days and ended by lysis. The most usual temperature was 101°F in the morning and 104° in the evening. The rash was seen in 85 per cent of the

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cases it appeared between the fifth and eighth days on the front and sides of the chest and abdomen and was maculo-papular the extremities were less affected than the trunk, and though it occasionally extended to the face it was less frequent there than was a general flush accompanied by injection of the conjunctivae.

In severe attacks euphoria was frequent at an early stage later there were muscular twitchings, stiffness of the neck delirium mania or even coma. Death was lasting 2-3 weeks was not uncommon.

The complications in approximate percentages, were pulmonary congestion 60 infections myocarditis 45 suppurative bronchitis 20 bronchopneumonia 9 pleural effusion 4 pulmonary emboli and thrombophlebitis each 1 (The name infectious myocarditis used in the above list of complications seems to be misleading from the text it appears that the cardiovascular complications are attributed to three different causes damage to the myocardium damage to the peripheral blood vessels and damage to the motor centres. The authors state that Peripheral vascular failure may occur independently of, or associated with congestive heart failure. It is our opinion that complicating peripheral failure is of central or peripheral origin and is due to a specific action of the concerned toxin on the cardiovascular complications peripheral vascular bed. They also state that cardiovascular complications occurred in 20 per cent. of the first 101 cases and 70 per cent of last 69 cases so that presumably the term infectious myocarditis is used without prejudice to the exact classification of the condition.)

Leucocytosis occurred only when there were complications otherwise there was leucopenia or a normal count. The sedimentation rate was increased to a varying degree its only significance seems to be that a slow return to normal progressed *pari passu* with the patient's restoration to health so that the rate might be useful as an index of recovery.

In the first 100 cases *Proteus* OXX was agglutinated at high titres second 100 the titres were much lower so that a rise of titre from 0 to 1-4 to be regarded as diagnostic. The authors suggest that the change was a variation in the antigen. They also state that positive reactions occurred as early as the ninth day and as late as the 38th.

Lumbar puncture was done in six cases because of severe cerebral manifestations in three of these the fluid was found to be at high pressure (20-30 mm water) and by withdrawing about 30 cc of fluid the pressure reduced to 120 and the symptoms were greatly relieved.

The fatality rate was 10 per cent it was much higher than this among patients arriving from the combat zone and among those belonging to the higher age groups. Of 13 officer patients six died four of these were more than 35 years of age.

Convalescence was prolonged neurasthenia weakness, dyspnoea and tachycardia persisted for 2-3 months on the average. Treatment was largely symptomatic. Incipient peripheral vascular failure was treated by oxygen vasomotor stimulants (peripheral or central) and blood plasma. For congestive heart failure double-concentrated plasma given by repeated small intravenous transfusions and digitalisation were used. Sulphadiazine or sulphathiazole had excellent effect in pneumonia the former failed in one case and penicillin was given intramuscularly in doses of 20,000 units every four hours to a total of one million units with good result. Penicillin had no demonstrable effect in a case in which there were no complications. Convalescent serum was given intramuscularly to two patients early in the disease in daily doses of 25 cc. for five days there was no apparent benefit.

John D. Meyer

HARRELL G T VENNING W & WOLFF W A. The Treatment of Rocky Mountain Spotted Fever with particular reference to Intravenous Fluids. A New Approach to Basic Supportive Therapy *J Amer Med Ass* 1944 Dec. 9 v 128 No 15 929-34 3 charts. [13 refs]

The authors challenge the views of distinguished workers like TOPPING [*Al Clin N America* 1943 v 27 722 and this *Bulletin* 1943 v 40 837] and PARKER who have suggested that intravenous medication does more harm than good in Rocky Mountain spotted fever. They claim that excellent results are obtained when laboratory procedures are used to control the type and amount of the injections.

Three cases are described to show the methods employed. In one case transfusions of saline and glucose were given by the intravenous route daily for nine consecutive days in quantities ranging from 1 000 to 2,500 cc in addition to the oral administration of 2 400 to 3 700 cc. of fluid. Plasma or blood was also given to this patient on five occasions in doses of 450 to 1 000 cc. by the vein. In this case the large intravenous doses of salines and glucose were thought to be causing oedema and deterioration of the patient's general condition but when blood and plasma were given the oedema promptly disappeared.

From the details given in the charts of the elaborate tests that were repeatedly carried out it is obvious that the treatment was controlled in a manner that would be quite impracticable in ordinary hospitals or in field conditions.

The general claim is made that the collapse of the peripheral circulation which occurs in the disease corresponds to a condition of shock and that full doses of plasma or blood are needed. Saline and glucose solutions when given alone may do more harm than good because they tend to reduce the already depleted protein content of the blood.

The use of convalescent blood or plasma did not appear to have any advantages over normal blood fluids.

[This paper is of special interest at the present time because the general lines of treatment of Rocky Mountain spotted fever must correspond closely with those suitable for the other fevers of the typhus group.]

John W D Megaw

YELLOW FEVER.

LINHARES H. Substâncias antibióticas. Ação dos filtrados de cogumelos e bactérias sobre o vírus amarelo neurotrópico [*Antibiotic Substances. The Actions of Filtrates of Moulds and Bacteria on Neurotropic Yellow Fever Virus.*] Reprinted from *Hospital* Rio de Janeiro 1944 Sept. 327-97 8 charts [394 refs] English summary

Filtrates of cultures of *Aspergillus flavus* *Penicillium camemberti* and a species of *Actinomyces* were found to have a lethal effect upon the neurotropic strain of yellow fever virus both *in vitro* and *in vivo*. When a virus suspension was mixed with filtrate and immediately inoculated into mice intraperitoneally (together with an intracerebral injection of starch) a high proportion (up to 80 per cent. in some cases) of animals survived. Similar results were obtained when the virus and filtrate were inoculated after standing in contact for one hour. Filtrate was also inoculated 2-4 hours before the virus or 24 and 4 hours before and on the two following days. In both series of experiments similar protection was observed. The results are based upon the inoculation of over 6 000 mice: full controls were used and the differences in death rates between experimental animals and controls were striking.

The virucidal principle first appeared in filtrates of seven-day-old cultures and attained maximum concentration between the 7th and 12th day: this is

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80 cc. had the same tryptic digest composition and this culture was of 18-hour incubation. It was found experimentally that an addition of 3.3 cc. of 23 per cent NaOH per litre produced the optimum initial pH of 8.8 in the medium and this amount of alkali was used as routine without further attempt at adjustment. The final pH after growth varied between 5.5 and 6.5. A very important part of the technique to produce massive growth was aeration by CO_2 followed in the earlier experiments by nitrogen and in the later ones by air with a special cloth bag device to obtain fine diffuse instead of coarse bubbles. A maximum growth could be obtained on this medium already in 24 hours. After removing the organisms the liquid part of the culture was readily freed from the inorganic salts and casein digest, leaving the soluble bacterial products of high molecular weight in pure form. B. F. Harvey

JENNINGS R. H. & LINTON R. W. The Biochemistry of *Vibrio cholerae*. II. The Influence of Environmental Factors on Growth. Arch. Biochem. 1944 Feb. 3 No. 3 429-33 2 figs.

In this continuation of the first article above the problems of composition of the medium are presented in more detail. (1) *The Influence of Glucose*. The higher the concentration of glucose the more rapid and more prolonged was the growth. An upper limit of consumption of the sugar was found to be 0.3 per cent when growth ceased because of the accumulation of acid. Any excess of glucose was not utilized. (2) *The pH Changes during Growth*. Optimum growth occurred between 6.0 and 8.0. Periodic neutralization of the medium with alkali during growth gave no increase of the vibrio crop. Thus the conclusion was reached that the buffer value of the medium would be all important in determining the final crop. (3) *Ammonium Sulphate as a Buffer*. The ammonium sulphate was originally intended to supply nitrogen for the growth of the vibrios but its activity was largely that of buffering and it "greatly increased the amount of CO_2 which the medium could neutralize." (4) *The Influence of Aeration*. That this was not due to mechanical action or removal of some objectionable volatile substance was tested by substitution of nitrogen for air. It proved efficacious. Aeration provides the proper concentration of dissolved gases for optimum growth. An important factor is the presence of sufficient concentration of CO_2 which should be greater than the normal CO_2 content of air. (5) *Casein Digest as a Nutrient*. This serves as a source of organic nitrogen and as a growth stimulant. It was more acceptable for the subsequent treatment of the culture than the equally effective 0.2 per cent. peptone. W. F. Harvey

JENNINGS R. H. & LINTON R. W. The Biochemistry of *Vibrio cholerae*. III. Acid Regulation by means of the Carbon-Dioxide-Bicarbonate Buffering System. Arch. Biochem. 1944 July 4 No. 3 311-18 1 fig.

It has been found that growth of *Vibrio cholerae* depends on the glucose present in the medium and it is well known that the vibrio requires maintenance of a high pH in its nutrient medium while acidification, or lowering of pH, brings growth to a stop. Unfortunately the utilization of glucose for growth results by fermentation in the production of acid. Earlier workers have aimed at keeping down this acidification by having CaCO_3 present in the medium. Under the conditions of experiment by the authors which involved continuous aeration of a very simple medium this addition did not result in greater yields of vibrios. The object of the authors was to obtain such a heavy growth in a water-clear medium that it could be used as vaccine, which they call the Biochemical Research Foundation (B.R.F.) direct vaccine. This medium was prepared as follows: a 3-litre flask provided with a...

and sampling tubes containing 1 litre of distilled water and 15 cc of casein digest and stoppered with cotton was autoclaved when it had cooled 10 gm of glucose dissolved in a minimal amount of water and 12 gm. of sodium bicarbonate were added and the mixture shaken until the bicarbonate had dissolved. As there was some formation of carbonate CO_2 was bubbled through for a few minutes before inoculation. Inoculation was effected by adding 100 cc. of a vibrio culture which had grown in the author's salt-C D [casein digest] medium [see above I & II]. An efficient buffer system was utilized in the medium to retard acidification. This buffer mechanism was based on the establishment of a carbon dioxide exchange system similar to that in the lung and depended on the fact that a considerable reserve of alkali in the form of sodium carbonate can be maintained at a desired pH by proper adjustment of the carbon dioxide content of the atmosphere. Aeration of the medium was effected by a cloth bubbler device and CO_2 from a cylinder was mixed with the entrant compressed air. Titration of the culture for its reaction could be done without interruption of aeration as also could the estimation of degree of growth. Periodic addition of alkali had been ruled out because the vibrio is immediately sensitive to even transient exposure to high alkalinity. The cholera vibrio could utilize greatly larger amounts of glucose in this new medium than in the old, but utilization did not altogether mean continuous growth. An optimum concentration of glucose for growth purposes and complete utilization was 10 gm. per litre (1 per cent). If 20 gm were used about 7 gm. still remained unused after multiplication ceased. This new method gave a fivefold increased yield of cholera vibrios. The culture was killed by the addition of phenylmercuric acetate and could be used directly as a vaccine or as a readily purified source of vibrios for chemical and physical studies.

W F Harvey

PAUL, B M & CHATTERJEE B C Pyrogenic Reactions following Intravenous Saline Infusions. *Indian Med Gaz* 1944 July v 79 No 7 305-7

Experiments were made in rabbits and in cases of cholera in which intravenous injections were given of hypertonic or normal saline of various pH values and made with either freshly prepared distilled water or tap water. These indicate that febrile reactions are produced by pyrogenic substances which are absent from freshly distilled water but present in tap water or by solutions of high or low pH but not by those about the neutral point. If the solution is more acid or alkaline than the blood can buffer pyrexia is produced.

Charles Wilcocks

BACILLARY DYSENTERY

FELSEN J Bacillary Dysentery Enteritis and Colitis. *Clinics* 1944 Oct v 3 No 3 535-52 11 figs. [12 refs.]

World-wide surveys carried out since 1933 by the Dysentery Registry reveal conclusively that where infectious diarrhoeas are carefully studied the majority appear to be bacillary dysentery.

In the United States in 1933 the reported incidence of this disease was 625 for unclassified diarrhoeas 17 043 for typhoid and paratyphoid 23 349 and for amoebiasis 1,573. Since then a steady and rapid increase in the bacillary dysentery returns has been accompanied by a striking decline in the unclassified

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dysenteries typhoid and paratyphoid, whilst amoebiasis remains uniformly low. But competent observers believe that the reported incidence is but a fraction of the actual incidence.

The remainder of this paper is devoted to a consideration of the pathogenesis and clinical aspects of bacillary dysentery. In acute bacillary dysentery the toxins produced within the lumen are absorbed through the intestinal wall and distributed throughout the body by the circulating blood to be eventually excreted in a reverse direction through the intestinal wall into the lumen of the bowel. The intestinal lesions are produced during the process of reverse excretion. The anatomical basis for this mechanism is simple. The intestines contain numerous solitary lymph follicles located partly in the mucosa and partly in the submucosa. The intramural mesenteric vascular arborisations terminate as delicate filamentous networks about the size of capillaries, which embrace and penetrate the lymph nodules—an arrangement which assures intimate contact between noxious agents which pass through the capillary wall, and the lymphoid tissue. A three-stage progression of pathological changes can be observed on the first, second and third days of the disease—punctate follicular hypertrophy and hyperplasia, punctate follicular necrosis discrete and confluent ulceration, and these changes can readily be seen through the sigmoidoscope.

During the first stage the enlarged lymph follicles bulging through the mucosa, appear to the naked eye as scattered grains of sand on a hyperaemic mucosa. In asymptomatic types they may not progress beyond this stage. In the average acute case the necrotic centres of the lymph nodules appear like the mouths of tiny diverticula. Then these areas of necrosis gradually become confluent and present the stereotyped picture of bacillary dysentery. Milder cases are just as infective as those which progress to extensive ulceration. All contacts, therefore, should be examined by sigmoidoscopy and culture. There are no healthy carriers of bacillary dysentery and a patient who excretes dysentery bacilli will always be found to have intestinal lesions.

Receding signs and symptoms do not necessarily run parallel to the healing of intestinal ulcers and the latter may persist for weeks. Recurrences are due to persisting lesions.

Acute bacillary dysentery is primarily an enterocolitis with predilection for the distal ileum and colon and it is stated that chronic distal ileitis (regional ileitis) is the end result of acute ileal involvement just as chronic ulcerative colitis is the terminal phase of colonic involvement.

P. Manson-Bahr

WARIN R P & ALEXANDER R S Splenomegaly in Bacillary Dysentery [Memoranda.] *Brit Med J* 1945 Feb 10 187

Splenic enlargement was present in 50 (57.7 per cent) of 866 cases of bacillary dysentery admitted to a general hospital in the Middle East between August 1943 and January 1944. There appeared to be no other cause than dysentery for the splenomegaly. Clinically the dysentery was mild or moderately severe diarrhoea lasting for 2.88 days on the average and the temperature returned to normal after 48 hours. Of 31 cases in which a culture was made the Flexner bacillus was grown in 13 (Flexner I in three cases, Flexner II in six cases and undetermined type in four cases) and in 18 no pathogens were found. The spleen was palpable on the day of admission in 49 cases. It was one finger breadth below the ribs in 37 patients, two fingerbreadths in 10 and three fingerbreadths in three patients. It remained palpable for 2-6 days in 43 patients and in the other seven it remained palpable until their discharge on the 15th to 18th day. The leucocytes of the blood showed no abnormality. The authors do not know the cause of the splenomegaly but think it was—

as Major R. S. ILLINGWORTH informed them that he had seen it in a similar proportion of cases of diphtheria tonsillitis, scarlet fever and measles in the Middle East and could find no cause for it.

J F Corson

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

PAYNE A. M. M. Amoebic Dysentery in Eastern India. *Lancet* 1945 Feb 17 206-9

In two years experience in Eastern India both in forward areas and base hospitals 2 000 cases of dysentery were seen of which 1 000 were amoebic. Except in a few cases of hepatic amoebiasis the diagnosis of amoebic dysentery was not made unless *Entamoeba histolytica* was demonstrated in the stools or typical ulcers seen in the gut.

Bacillary dysentery was diagnosed on the presence of typical bacillary exudate. Shortage of equipment precluded the use of cultures for diagnosis on any large scale so those which showed an indefinite exudate were grouped as clinical dysentery. Some were doubtless cases of healing bacillary dysentery and others of amoebiasis with very scanty protozoa in the stools. The proportion of types of dysentery are given in a table —

Source of cases	Diagnostic procedure	No	Bacillary dysentery	Amoebic dysentery	Clinical dysentery
Consecutive cases passing through	One stool exam. Case evacuated to base hospital	149	27 (18%)	47 (31.5%)	75 (50%)
Base hospital	Stool exams. with sigmoidoscopy in few cases	380	196 (36%)	193* (51%)	51 (13%)
Base hospital	Sigmoidoscopy and stool exams.	500	163 (33%)	282† (56%)	55 (11%)

*Includes 27 double infections. †Includes 38 double infections.

Amoebiasis was $1\frac{1}{2}$ times as common as bacillary dysentery. The stay in hospital in amoebiasis varied from a minimum of three weeks up to several months usually 28 days in uncomplicated cases whereas in bacillary dysentery the stay was 7-14 days usually 8 days. The time lost from dysentery in one unit over a period of eight months averaged 27 days in cases infected with *E. histolytica* and 2-3 days in those not so infected. The mortality from amoebiasis was 0.8 per cent. whereas no death occurred from bacillary dysentery in nearly 700 cases.

Both conditions appeared to be mainly fly borne for instance owing to the use of wet fuel and an unsuitable incinerator in one unit large numbers of flies bred in unburned faecal matter and invaded the cookhouse 100 yards away with the result that seven cases of amoebic dysentery occurred among 100 men 4-6 weeks after this disaster.

All grades of severity were seen from the very acute with extensive ulceration 20-30 daily stools fever and prostration to the mildest diarrhoeas. One case

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of extensive ulceration without diarrhoea or obvious blood or mucus in the stools was recorded. The patient was also heavily infected with subtertian malaria.

At autopsy general peritonitis with thick fibrinopurulent exudate in the right iliac fossa was found. There was perforation of the greatly thickened caecum. Intrinsic massive confluent amoebic ulceration was seen there and scattered ulcers in the ascending colon and sigmoid.

Amoebic typhilitis closely mimicking appendicitis also caused concern. The complaint was pain in the right iliac fossa, either colicky or continuous often occurring after meals presumably as a result of the gastrocolic reflex. There was usually diarrhoea with blood and mucus but the most difficult cases were those in which the stools were formed and without mucus. The temperature might be raised to 99-100°F. Tenderness guarding, rigidity, greatest over McBurney's point may cause suspicion of appendicitis. A thickened caecum is a valuable sign and also liver tenderness. Rovang's sign (pain in the right iliac fossa on pressure in the left hypochondrium) and a reduced or absent abdominal reflex may all be found but are inconstant.

Rectal examination may elicit tenderness on the right side sometimes there is a "retrety touch" and the mucosa is folded redundantly. There may be blood or mucus on the withdrawn finger. The white cell count shows an increase to 10,000-14,000 but the polymorphs are not increased relatively to other cells. If hepatitis is present the total count may be higher though it may be normal and the polymorphonuclear leucocytes retain their normal proportions. Sigmoidoscopy showed typical leucons in some 50 per cent. Two cases of amoebic typhilitis were opened under the impression that they were appendicitis. Plastic peritonitis was seen but no perforation.

Amoebiasis causing dyspeptic symptoms occurred in chronic cases with pain in the epigastrium, or right hypochondrium, 4-2 hours after meals. Symptoms due to mild hepatitis or reflex pyloric spasm disappear rapidly under emetine treatment.

Amongst 1,000 cases of amoebiasis the following complications were noted —

Mild amoebic hepatitis	50 per cent.
Acute amoebic hepatitis	3.6 "
Hepatic abscess	2.8 "
Haemorrhage (severe)	0.2 "
Local peritonitis	1 "
Perforation (with general peritonitis)	0.8 "
Perforation (with abscess formation)	0.2 "
Rectal granuloma	0.2 "

Hepatitis was so common as to become part of the disease. Usually it was mild and responded immediately to emetine. The more severe forms were rarer and graded imperceptibly to liver abscess. They did not respond so quickly to emetine and tended to recur. Amoebic hepatitis without diarrhoea and with negative stools occurred in eight cases.

Of 28 cases of hepatic abscess 20 were in Indians—an unusually high proportion. Out of 700 British troops with amoebiasis 1.1 per cent. developed liver abscess. Out of 300 Indians the proportion was 8.6 per cent. There was one death in an Indian with an abscess secondarily infected with *Staphylococcus aureus*. Of the remaining 27 three were aspirated and all the remainder made good recoveries on emetine alone. The maximum dosage was grains 60 in 120 days. The average dose was grains 36 in 108 days. Severe haemorrhage occurred twice in one case associated with perforation and death. The others recovered with emetine and blood transfusion.

Perforation occurred seven times in the caecum and once in the descending colon. General peritonitis followed in six fatal cases where the gut was

gangrenous and too friable for effective closure two of these perforated during emetine treatment. Two perforations resulted in abscess formation behind the ascending colon. Both had secondary haemorrhage after drainage.

Amoebic granuloma of the rectum was seen twice at sigmoidoscopy with large cauliflower masses resembling carcinoma. They responded to emetine and eusol enemata.

As regards diagnosis the author maintains that the exudate in amoebic dysentery is not characteristic as an indefinite picture with necrotic pus cells and degenerated r b c. is seen in healing bacillary dysentery. Charcot Leyden crystals are a guide but were found in non-specific ulcerative colitis and in carcinoma.

With sigmoidoscopy and microscopy of fresh specimens an immediate diagnosis can be made in 80 per cent. of cases. Proctoscopy if performed gently is painless and of more value than is generally recognized as 50 per cent. show lesions in the rectal ampulla. Premedication before sigmoidoscopy is unnecessary unless the patient is very nervous. The knee-elbow position was used for preference.

Results of 500 Sigmoidoscopies

Type of dysentery	Cases	Positive	Negative
Bacillary	163 (32.6%)	160 (98%)	3
Amoebic dysentery (final diagnosis)	232† (56.4%)	226 (80%)	56†
(1) Appearance diagnostic	—	155 (55%)	—
(2) Appearance not diagnostic	—	71 (25%)	—
diagnosis by stool exam.			
Clinical	53 (11%)	—	55
Total	500	386 (77.2%)	114

†Includes 38 double infections. ‡Diagnosis by stool examination.

Treatment was very largely dictated by the drugs available. For a primary case 10-12 injections of emetine grain 1 (total given being grain 1 to 1 stone body weight). The injections were divided into two groups of 6 with three days rest in between to diminish toxic cumulative effects. Then carbarsone 0.25 gm. b.d. was given by mouth for 10 days.

This achieved clinical cure in 50 per cent. (but the author thinks this may be an overestimate). In 40 per cent. cysts were found within three weeks and though carbarsone appeared to clear most of these 10 per cent. required further emetine or E.B.I. plus chiniofon enemata. Two per cent. resisted all forms of treatment.

Cysts seldom reappeared in the faeces until 10-20 days after treatment.

It was felt that if three courses had been given a further course would be unlikely to cure so those patients were sent to special centres for the combined treatment with E.B.I. and chiniofon retention enemata.

Relapses became more frequent and more resistant to treatment the longer the infection had lasted. More thorough treatment of the initial attack including the combined treatment might reduce the number of chronic resistant cases. Sulphapyridine or sulphaguanidine in four-day courses were of great assistance in allaying symptoms but did not affect the amoebae.

Various other drugs—kurchu bismuth iodide. Enterosol (4-3 iodoxy quinoline). Amoebarsan (similar to carbarsone). Stovarsol retention

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emetics of emsol, silver nitrate and "Argyrol" were of some but inferior value. Kurchi was of little value. Myocardial damage from excessive doses of emetine may be missed, if the pulse is not examined after suitable exercise. Response to the erect position may be dramatic and may be associated with cyanosis, breathlessness and faintness. Personal idiosyncrasy is important and myocardial damage is more common in relapsed cases. A falling pulse-pressure is an early sign. Mild cases clear up in 4-6 weeks. E.B.I. can contribute to cardiac damage though less liable to do so than emetine.

Diarrhoea in emetine and E.B.I. treatments is not uncommon and must not be interpreted as a relapse of dysentery. Diet makes little difference to treatment. Results of treatment could only be estimated as the majority of cases could not be followed up.

Results.

Clinical cure
Improved with clinical relapse
Frequent relapse
Resistant cases
Death

33 per cent.
33
23.2
5
0.8

These are very disappointing figures and there is grave need for new and more efficient drugs.

BOWFORD R. R. *Chronic Amoebiasis in Soldiers*. J. Roy. Army Med. Corps.
1944 Dec. v. 83 No. 6 279-83.

This paper describes the methods employed in diagnosis and treatment of cases admitted to a Military Centre for Tropical Diseases between November 1942 and January 1944. During this period 112 patients were admitted with provisional diagnoses of dysentery or its effects. Of these 28 gave a reliable history but no pathogenic organisms or protozoa were found in the stools. 51 were found to have bacillary dysentery (including acute Sonne dysentery) by isolation of the organisms. 33 were considered to be suffering from amoebiasis of these 17 were officers and 16 other ranks. One had never been out of the United Kingdom and appeared to have become infected in Northern Ireland. The length of history varied from two months up to ten years. Out of these 33 in seven only was recent diarrhoea the principal symptom. In a few others it had been occasional, but in 14 it was absent altogether. Four had hepatitis two with diarrhoea and two without.

Diagnosis was suggested by history of previous dysentery, previous residence in the tropics and sub-tropics, the presence of tenderness over the colon or liver, the naked-eye appearances of the stools, which were occasionally characteristic with blood, mucus and typical odour but often watery and unformed.

Diagnosis was confirmed by—
(1) *Microscopic examination of the stools*.—Vegetative *E. histolytica* were found in six and cysts in 24. In searching for the latter much assistance was obtained from Faust's zinc sulphate concentration method. At least three stools were examined by ordinary and three by the concentration method.
(2) *Microscopical examination of specimens obtained at sigmoidoscopy*.—Scrapings were taken with a Volkmann's spoon through the sigmoidoscope, should be lubricated with vaseline as the presence of oil droplets makes the scrapings useless for microscopic examination. No amoebae were ever found in specimens obtained from an unbroken surface but were demonstrated

in smears of bloody mucus seen coming down the sigmoid when no ulceration was visible. In two cases active amoebae were found in scrapings from ulcerations after repeated examination of stools had failed to demonstrate them or their cysts.

(3) *Sigmoidoscopic appearances*—One case only was diagnosed on sigmoidoscopic appearances alone. This patient gave a history of previous amoebic dysentery followed by mild diarrhoea and aching abdominal pain. He also had a moderate leucocytosis. With specific treatment the symptoms were relieved and the colon returned to normal.

(4) *Response to empirical therapy*—With this exception patients complaining of diarrhoea and colonic symptoms with negative faeces and sigmoidoscopic scrapings were not benefitted by specific antiamoebic treatment.

Of the 30 cases in which treatment was recorded 20 had been treated previously for amoebiasis and 10 had not. Of these 20 seven had received emetine injections repeated on several occasions. Only seven had previously received an efficient course of E.B.I. and chiniofon retention enemata. Several more had been treated at various times with emetine stovarsol and incomplete E.B.I. and chiniofon enemata.

The drugs available are emetine emetine-bismuth iodide auremetine [combined emetine and auramine periodides] chiniofon stovarsol or carbarsone and it is generally agreed that E.B.I. or auremetine by the mouth are the most effective and that simultaneous E.B.I. or auremetine with chiniofon enemata probably give the highest proportion of permanent cures. Emetine injections usually abolish symptoms but effects are rarely permanent.

In treatment of these cases emetine injections were used for two purposes for the treatment of hepatitis in which 12 daily injections were given intramuscularly and to control diarrhoea in patients with active dysentery before other treatment was commenced for which three or four injections sufficed. All patients were treated with a course of E.B.I. by mouth and chiniofon retention enemata for 12 days followed by stovarsol for 10 days. The minimum dosage given to those who had received no previous treatment, was E.B.I. grains 2 nightly with 300 cc. 2½ per cent. chiniofon enemata retained for at least six hours.

The maximum dosage to those in whom this treatment had failed before was E.B.I. grains 3 nightly and 300 cc. of 5 per cent. chiniofon but most had six days of the lower dosage followed by six days of the higher. Stovarsol was given in doses of grains 4 twice daily. This treatment was rarely depressing. In a few it failed. In the remainder there was noticeable improvement in colour and general condition with relief of symptoms. One developed a generalized maculo-papular rash whilst taking stovarsol.

The immediate results were on the whole satisfactory in the case of officers and unsatisfactory in other ranks. Of 16 other ranks treatment failed completely in three cysts were still present and symptoms for all practical purposes unaltered after two complete courses of E.B.I. chiniofon and stovarsol and in two of them an additional course of auremetine gram 1 four times daily for 10 days. In three more the stools were cleared of cysts for the time being but symptoms remained. All were discharged from the Service. The reasons for failure in treatment are not fully understood but possibilities should be considered—

(1) *Failure of co-operation on part of the patient*—Those who had treatment before had lost faith in treatment and only wanted to get out of the Army. They were difficult and disgruntled. It was possible that some of them endeavoured to evade treatment.

(2) *Failure of the coating of E.B.I. capsules to dissolve*—This is probably greatest in warm climates, and undissolved orange-coloured keratin-coated

capsules have been recovered from the stools of patients in this war. When keratin-coated capsules are used the stools should be strained through muslin, and if they are found, the capsules should be crushed and given in a spoonful of jam. A number of cases have been treated in this manner without producing undue nausea or vomiting. Such insoluble keratin-coated capsules have been used extensively in the Army and it is possible that they have been one of the causes of failures.

(3) *Possible induced emetine-fastness*.—Whereas the immediate results of treatment were highly satisfactory in all cases treated for the first or second time, all patients in whom it was unsuccessful had had repeated unsuccessful previous treatments. Therefore emetine-fastness is possible. It is wise to recommend that emetine injections should be used to tide the patient over for a short period till it is convenient for him to have the full combined treatment. Whenever possible the effect of such treatment should be checked by further examination of the faeces and by sigmoidoscopy. Thereafter the faeces should be re-examined in 3-6 months' time.

[That most of the points which he has emphasized now for over 20 years have been confirmed is a source of satisfaction to the reviewer. The failure of keratin-coated capsules of E. B. I. for instance, to dissolve in the bowel has been recorded by him as well as by many others ever since the introduction of this drug as a treatment for chronic amoebiasis. It is satisfactory too to learn that they have somewhat tardily been withdrawn from use in the Army for it is more than probable that many failures in treatment have been attributable to this cause alone. This paper once more confirms the fact that attention to details is essential for the successful treatment of amoebiasis, especially under war conditions.]

P. Venson-Bahr

WEKRICH D. H. *Studies on Dictyamoeba fragilis* (Protozoa). IV. Further Observations, with an Outline of Present-Day Knowledge of this Species. *J. Parasitology* 1944 Oct. v. 30 No. 5 322-38 49 figs. on 2 pls. [44 refs.]

The author who has studied the peculiar amoeba or aberrant flagellate *Dictyamoeba fragilis* for a number of years now gives a general account of this organism, based chiefly on the study of 100 cases of infection which have been diagnosed in his laboratory. He notes that for its identification, training in recognition is probably of more importance than for any other intestinal protozoan. Stained films are nearly always required. On this account the figures of its incidence in many surveys can hardly be regarded as accurate. The normal features of the amoeba are known but there are many departures from these. They are carefully described. A feature not hitherto recorded is the occasional formation of a peculiar tube-like extension of cytoplasm from the layer between endo- and ecto-plasm. It passes through the ectoplasm and protrudes from the body surface. Its function is unknown, but it is noteworthy that a similar structure occurs in *Histomonas meleagridis* to which, as noted by DOBELL [this Bulletin 1941 v. 38 422] *D. fragilis* shows many resemblances. The author holds that in mitotic division of the nucleus only four chromosomes are formed, whereas Dobell maintains there are six. The author agrees with Dobell that the desmose may persist till cytoplasm division occurs. Another feature of resemblance to *H. meleagridis* is the presence of a deeply staining layer of cytoplasm between the ecto- and endo-plasm.

The paper which is illustrated with 49 figures depicting the many structural variations described by the author requires to be studied carefully by specialists who undertake the identification of intestinal protozoa. C. E. Wenyon.

RELAPSING FEVER AND OTHER SPIROCHAETOSSES

BURROUGHS A L. & HOLDENRIED R. Recovery of Relapsing Fever Spirochaetes from *Ornithodoros turicata* (Duges), 1876, in California. *J. Bacteriology* 1944 Nov v 48 No 5 609

Relapsing fever has been transmitted to guineapigs by the bite of *Ornithodoros turicata* collected in California. The ticks (175) were collected from the burrows of *Citellus beecheyi* divided into 11 pools and fed on guineapigs. This is the first record that this tick has been found to be a vector in California.

Charles Walcocks

SCHUHARDT V T & O'BRYAN B E. Relationship of Penicillin Therapy to Brain Involvement in Experimental Relapsing Fever. *Science* 1944 Dec. 15 550-52.

The authors have tested the effect of penicillin on relapsing fever infection in rats using a strain of *Spirochaeta recurrentis* (novyi) which had only recently been derived from ticks *Ornithodoros turicata*. The 45 rats used were injected with small doses, 0.01 cc. of onset blood containing 1 to 5 spirochaetes per 100 dark fields and were divided into nine groups of five each. Five of these groups were treated with penicillin beginning some days after the blood had become positive in three groups treatment was begun on the first day of onset and one group was left as a control. The animals were subsequently examined for residual brain infections. The 25 rats in which treatment was begun late and the controls all showed residual infections including 7 out of 10 that had received more than 40 000 units of penicillin per kgm. In the early treatment group the brains of seven out of eight rats were negative. It would appear therefore that adequate dosage of penicillin about 40 000 units per kgm given early in the treatment of experimental relapsing fever will not only cause the disappearance of spirochaetes from the blood stream but will prevent residual brain infection in the great majority of cases. [Previous work (see this *Bulletin* 1944 v 41 942) showed that much higher doses are necessary to cure more intense infections.]

E Hindle

YAWS

HELFET A J. Acute Manifestations of Yaws of Bone and Joint. *J. Bone & Joint Surgery* 1944 Oct v 26 No 4 672-81 12 figs

This paper based on findings in West African cases mostly soldiers deals with acute lesions that require urgent treatment.

The onset was more rapid and more pain was suffered than in syphilitic lesions. Duration of symptoms was rarely longer than a week by which time marked bony changes might be present resembling septic lesions. In syphilis symptoms are less marked and less acute.

Onset was often related to trauma and was accompanied by fever rarely high and widespread rheumatic pains which lasted a few days. Localizing symptoms help in diagnosis.

The tibia femur clavicle and humerus were found especially affected but the skull and lumbar vertebrae were also involved and occasionally the bony lesions were generalized. Plantar and palmar lesions did not co-exist with bone lesions none of which had ulcerated through the skin. The Wassermann and Kahn reactions were positive in all cases.

X-ray films showed cortical thickening and bony expansion with localized areas of rarefaction or cortical rarefaction and periosteal bony deposits. These deposits might resemble those in osteogenic sarcoma or in the most acute lesions, the onion-layering of a Ewing's tumour (The illustrations are excellent.)

The histo-pathological appearances resembled those of syphilis in the small round cell and plasma cell infiltration and perivascular cuffing, but there was little or no endarteritis obliterans which is so characteristic of syphilis. Yaws lesions were more vascular than those of syphilis and it was suggested that this may account for their more rapid course.

Ganglia lined with oedematous granulation tissue and hypertrophied villous tags and chronic synovitis with hypertrophied synovial membranes were seen. [No note is made of the number of lesions observed or studied histo-pathologically.] Ganglia were excised before arsenical treatment was given as they subsided slowly.

There was dramatic response to treatment by Acetylsalicyl or Novarsenobillon (N.A.B.) or alternate doses of Bismostab and Sulphostab the pain disappearing in 1-2 weeks and bony lesions showing some resolution in six weeks. [Dosage not given.]

[The lesions illustrated are almost certainly all those of tertiary yaws but the criteria for differentiating from syphilis are rather weak. The most important diagnostic aids are a history of yaws scars of secondary skin yaws or failing these a rural origin of the patient. Similar lesions are likely to occur in any Colonial Service personnel from yaws areas. Medical Officers in charge of such will find this paper very helpful.]

C. J. Heckett

LOFGREN R. C. Yaws treated with Prulellin. Report of Case *US Nav Med Bull* 1944 Nov v 43 No 5 1025-30 2 figs.

A case of yaws in a white man was treated with penicillin with a very successful immediate result.

History.—The patient aged 20 was a ship's cook in the American Navy. In September 1942 he got gonorrhoea in British Samoa and was treated with sulphathiazole orally and with potassium permanganate irrigations. He denied having had penile sores then or at any other time and on entering the Navy in February 1942 his blood gave a negative Kahn reaction. In January 1944 in American Samoa, he burned his right forearm and a small ulcer developed and gradually became larger. At this time he had visited native huts and held naked children in his arms but he did not remember having seen sores on the children. He arrived back in the United States on March 7th, 1944 and on the voyage his ulcer was treated with ointments but continued to enlarge. On April 4th he noticed a red purple on his cheek which became larger and pustular and covered with a yellow crust. A week later similar lesions appeared on his face scalp arms hands chest, back, legs and penis. He had no subjective symptoms.

Condition on examination.—He was seen by the author on April 18th, 1944 there was a generalized erythematous papular and pustular eruption with many of the lesions crusted and scaling, and some were on the palms and soles. Some of the papules were pitted where the crusts had fallen off, and on the right cheek there was a granulomatous nodule covered with a yellowish-brown crust which, when removed, disclosed a raspberry-like base. On the flexor surface of the right forearm there was an ulcer about the size of a half-dollar with a granulomatous base. There were a few erythematous erosions and papules on the penis and prepuce. The posterior cervical axillary epitrochlear inguinal and femoral lymphatic glands were enlarged. Spirochaetes resembling *S. pertenuis* were found by dark-ground illumination in preparations taken

from the forearm ulcer and other lesions. On admission to hospital his blood gave a strongly positive Kahn reaction the red cells numbered 4 290 000 white cells 4 050 with neutrophiles 54 per cent and lymphocytes 42 per cent. and haemoglobin was 85 per cent. The cerebrospinal fluid showed no cells protein 0.032 per cent. Kahn reaction negative colloidal gold curve normal. The diagnosis was yaws.

Treatment—On April 22nd he was given 20 000 Oxford units of penicillin intravenously and 15 000 units intramuscularly immediately afterwards then he received 15 000 units intramuscularly every three hours until a total of 1 500 000 units had been given during 12 days. Serum from the right cheek lesion was examined by dark ground illumination at 4 8 18 and 24 hours after the beginning of treatment spirochaetes were seen at 4 and 8 hours not at 18 and 24 hours. Four hours after treatment was begun all lesions even those which were apparently drying up had become more prominent and showed peripheral erythema, evidently due to a local shock reaction similar to a Herxheimer reaction in syphilis. The patient made no complaint and his temperature was normal. At 8 hours the lesions had become still more pronounced and additional erythematous macules had appeared especially on the face. At 18 hours this peripheral erythema had gone many crusts had fallen off and the lesion on the right cheek was smaller. During the next two days involution of the lesions proceeded rapidly and by the fifth day the yaw on the cheek and all the smaller lesions had entirely healed, and the forearm ulcer which had been having saline wet compresses was dry and almost healed and local treatment was stopped. By the 12th day all the lesions had healed his temperature which had been taken every three hours had remained normal throughout. The Kahn reaction was four plus on May 22nd, one plus on May 29th and negative on June 6th and 9th.

The author states that a prolonged follow up will be necessary to judge whether a permanent cure has been obtained.

J. F. Corson

LEPROSY

JUON M. *Les derniers cas de lèpre autochtone en Suisse. (The Last Indigenous Cases of Leprosy in Switzerland.)* *Schweiz med Woch* 1944 July 22 v 74 No 29 795-800

This paper is mainly of historical interest. In 1898 JADASSOHN discovered a focus of leprosy at Guttet the last case of which has now disappeared. In the middle ages Switzerland suffered severely from leprosy records of which still exist and in 1898 four cases were found in Guttet among persons who had never left their village since their birth constituting an endemic focus of the disease. Two were lepromatous cases in a brother and sister of 10 and 11 years of age one was a lepromatous case in a man of 47 and the fourth a mixed case in a youth of 17 all four patients were closely related, as shown by a genealogical table. These cases occurred among a population of 200 people in an isolated area. In the village of Feschel, not far away two other cases had occurred in one family and here the disease was traced back for one hundred years with a history of seven cases in four generations only two of which still survived in 1907 by which time three of the total of six verified cases had ended fatally. In 1921 three remained, but in 1922 two new cases were reported, making a total of five. Four of these are described in detail and illustrated by photographs two were advanced lepromatous and one a third-stage neural case. All these patients had died by 1927 thus bringing the disease to an end.

X-ray films showed cortical thickening and bony expansion with localized areas of rarefaction or cortical rarefaction and periosteal bony deposits. These deposits might resemble those in osteogenic sarcoma or in the most acute lesions, the onion-layering of a Ewing's tumour [The illustrations are excellent.]

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The persistence for so long of this focus of infection is attributed to the poverty and backward social and hygienic conditions of the inhabitants of these remote villages
L. Rogers.

Muir, E. Leprosy in Antigua. (2nd Report.) *Leprosy Review* 1944 Dec. v 15 No 2, 35-40

At this Dr Muir's second visit in July 1944 he is able to report some progress since his first inspection in January 1942 (see this *Bulletin* 1943 v 40 463). Changes have been made in the Leper Act and Rules on the lines recommended in the former report and there has been more following of contacts leading to earlier segregation of infectious cases. This is shown by an increase in the leper home of L1 and L2 cases from 2 to 13 and of L3 cases from 18 to 19 accompanied by a decrease of active nerve cases from 11 to 8 and an increase of the total cases from 37 to 48. In addition arrangements have been made to place 27 closed neural cases under treatment outside the home. Another 14 arrested cases are living in their own homes under supervision. The total known cases now number 80. Improvements have also been made in the staff, including the provision of a matron with two years training at the Trinidad Leper Settlement. The patients have gardens but their diet is still deficient in vegetables and fruit. The cost of segregation amounts to £52 a head annually including £24 for food. The control of leprosy by up-to-date methods is thus important from the financial as well as from the public health point of view. The difficulty in supplying a properly qualified staff for combating leprosy in such a small island as Antigua and most of the West Indian Islands is pointed out and although the Trinidad settlement is prepared to take a certain number of cases suitable for treatment there remains the difficulty in persuading patients from other islands to avail themselves of this offer.

L. Rogers

Muir, E. Leprosy in St. Kitts and Nevis. (2nd Report.) *Leprosy Review* 1944 Dec. v 15 No 2 40-43

In July 1944 Dr E. Muir paid a second visit to these islands to see the results of his report on his first visit in February 1942. (see this *Bulletin* 1943 v 40 35). A new Master of the Leper Home has been appointed after being trained the Trinidad Chacachacare Leprosarium with advantage, but little other progress appears to have been made. The total cases in the home have only risen from 46 to 49 by the addition of three neural cases. The active lepromatous cases remain at 27 but the new admissions amount to 13 because 10 patients have died in the interval between the visits. There are however about 27 known active cases including 7 or 8 lepromatous ones outside the Home, and other cases isolated at home require more supervision. The surgery premises are inadequate a treatment room with running water being badly needed and more land is needed for cultivation by the inmates. Several of the nerve leproides might be cleared up by intra-dermal treatment this also applies to extramural cases. The fact that some fresh cases were detected during a short visit indicates that there are still active cases at large. No mention is made of the regular examination of contacts which is essential for detecting new cases in an early stage.

L. Rogers.

Muir, E. Second Report on Leprosy in Jamaica. *Leprosy Review* 1944 Dec. v 15 No. 2, 43-8.

This visit was made in October 1944 to follow up the results of a former one
ds

it produced, it never became very popular. Later chaulmoogra oil was used, with a diet rich in vitamins and with yeast tablets. Treatment with diphtheria antitoxin and toxoid, on Oberdoerffer's theory was tried but the results were disappointing. Of 28 whose sera were tested by the Wassermann and Kahn reactions 11 were positive to both, 10 were negative to the former and 12 to the latter while five and three respectively were doubtful.

A graph shows the number of cases and the population for the years 1899-1944. The year of greatest number was 1878 when the total was 61 of whom 15 were in Curaçao 28 in St. Eustatius and 18 in St. Martin. On January 1st 1944 there were 27 in the leprosarium, 18 males, 9 females. All but five were blacks, four were whites and one a half-caste. Presence of the disease was detected in one under 5 years in five between 10 and 15 in four between 15 and 20 in three between 20 and 25 in one between 25 and 30 in four between 30 and 35 and in nine above that age. As regards type of case, eight were nodular four nervous, four were macular and 11 were of the mixed type.

Discharge from the leprosarium was permitted if bacteriological examination was negative for three consecutive years. H. Harold Scott.

MOXLEY T. D. F. Abstract of a Further Report on the Off River Leprosy Settlement, Nigeria. *Leprosy Review* 1944 Dec., v 15 No. 2, 50-52.

This report on the work of 1938 to 1943 amplifies the information in one that was reviewed in this *Bulletin*, 1944 v 41 537. This settlement deals with the Onitsha Province of Nigeria with a population of over one million in 5 000 square miles. In 1943 the central settlement provided residence for 1 187 patients, all highly infective except for some advanced nerve cases requiring special care. In the surrounding territory a number of out patient clinics provide regular treatment for from several hundred to one thousand earlier cases at each with a total yearly attendance of 305 783. The province is estimated to have from 20 000 to 25 000 active cases, of which 3 000 to 5 000 are highly infectious requiring isolation. Some live in villages in which only infectious patients reside, and many more are isolated in their homes.

The child adoption scheme of B.E.L.R.A. provides for about 100 infected children in a special compound, and others are paid for by their parents. The indications are that few patients with active disease fail to attend the clinics in order to obtain treatment, but full surveys have not yet proved possible. Bacteriological examinations of 372 cases in 1941-43 showed negative throughout 79.2 per cent positive throughout 9.4 per cent. becoming negative 9.2 per cent. and becoming positive 2.2 per cent. The work has steadily increased in spite of war time difficulties. L. Rogers.

DEKSHAM W. The New Lnapula Leprosy Settlement, Northern Rhodesia. [Abstract.] *Leprosy Review* 1944 Dec. v 15 No 2, 53-5.

This is a note on the early stages of the organization of a new leprosy settlement in the densely populated Lnapula Valley of Northern Rhodesia, a little south of the Belgian Congo border by an experienced Toc H worker under the superintendence of the doctor in charge of the neighbouring hospital of the London Missionary Society. Buildings are being erected to accommodate 500 patients with 5 000 acres of land, together with outlying clinics for early cases. Within eight months over 113 cases have been examined and 60 are attending for injections, and it is hoped to admit 100 patients to the settlement shortly to make a start in meeting the needs of a hitherto untouched area.

L. Rogers

SANTRA I *The Problem of Leprosy in the Tehri Garhwal State U P Leprosy in India* 1944 Oct. v 16 No 4 118-22

Tehri Garhwal is an Indian State (Himalayan) situated at the extreme north west corner of the United Provinces. Like all the Himalayan area it has a much higher leprosy rate than that of the adjoining plains on account of its more humid climate at least 138 cases of leprosy from this State were recently found in leper asylums of British India. In 1916 the State authorities began to control the disease and were helped by an ancient custom of using some kind of segregation of advanced cases on the outskirts of the villages. In 1916 orders were issued to enforce village isolation more rigorously and in case of failure the patients were taken by force to a colony opened at Barahat and were maintained there at the cost of the relatives but early in January 1917 only 19 inmates were found there in place of an expected number of 117 owing to the failure of the relatives to pay for their upkeep. In 1919 it was ordered that the relatives of the patients should contribute a fixed amount of food when the harvest was ripe or pay an equivalent in money but this plan also appears to have failed as there were no cases at Barahat recently.

In 1943 the State authorities asked for the help of the Indian branch of B.E.L.R.A. and a research worker was sent to make a study and a survey of villages known to be infected, with the result that an incidence of 2.05 per cent. was found among 7082 people examined. Of 117 cases 45 per cent were infectious. A colony at Mumikirti provides accommodation for 157 cases without treatment. Children up to 14 years formed only 4.2 per cent. of the whole and mild tuberculoid cases 20 per cent. Only 16 patients were found to have been isolated outside villages 11 of them with uninfected neural lesions. It is advised that only infective cases should be admitted to the Mumikirti colony under the charge of a medical man trained in leprosy work who could carry out treatment.

L. Rogers

SHAMA RAO A *Leprosy Surveys in Hyderabad, Deccan. Leprosy in India* 1944 Oct. v 16 No 4 123-7 1 map

These surveys were carried out within a radius of five miles around existing leprosy clinics. The incidence in the four districts dealt with varied between 0.24 and 0.36 per cent. it was greatest in the lower castes. Lepromatous cases varied between 23 and 47 per cent. and the proportion of children under 15 years of age was below 10 per cent. in all the districts. The number of cases found was from 6 to 30 times as high as the figures for these districts returned in the 1931 census. The author concludes that leprosy is not a particularly serious problem in the Hyderabad State.

L. Rogers

SHAMA RAO A. *A Simple Method for the Preparation of Iodized Hydnocarpus Oil. Leprosy in India* 1944 Oct. v 16 No 4 116-17

The author quotes the method of preparation of iodized hydnocarpus oil recently advocated by DHARMENDRA and SANTRA (see this *Bulletin* 1944 v 41 1045) and points out that it is not practicable for an officer travelling with little equipment. He therefore used the following simplified method of preparation with satisfactory results—40 grams of pure iodine are added to 1 oz 2 dr of pure ether in a 2 oz. stoppered bottle and shaken well for about a minute. The iodine dissolves and the iodized ether is added to 1 lb. of sterilized and cooled pure hydnocarpus oil. On shaking, the resulting iodized oil is of a brown colour and can be used immediately for injections. On exposure to air or sunlight, the oil loses its transparency and becomes of a dirty green colour after two weeks but does not show the presence of any free iodine and no

precipitate form. Although the author prefers to use the freshly prepared iodized oil, he found the green samples equally effective in treatment and either may be injected subcutaneously or intradermally twice a week in the usual doses the freshly prepared iodized oil is easier to inject than the pure oil. He has used this method for four years in a very large number of cases of leprosy early cases of both types respond favourably *L. Rogers*

DEGOTTE J. Recherches sur l'activité thérapeutique de l'huile essentielle de citronnelle dans la lèpre. [Essential Oil of Citronella in Leprosy] *Leprosy Review* 1944 Dec. v 15 No 2, 28-35 1 fig

The author working in the Belgian Congo during the war was unable to obtain sufficient supplies of chaulmoogra oil, so he sought for a substitute. Thus he found in an oil of somewhat similar constitution obtained from a common Congo plant belonging to the family Cymbopogon from the thick leaves of which it is distilled, and it contains 85 per cent. of a mixture of geraniol, citronellol, citral and citronellal. The remainder is mainly terpenes. It is sterilized by heating on a water bath for one hour. To diminish its irritant properties one part is diluted with nine parts of cotton seed oil, when it can be injected either subcutaneously or intramuscularly in doses of 1 cc. in the first week, 2 cc. in the second, and 3 cc. per week in the subsequent ten weeks. After an interval of fifteen days the course is repeated. In larger doses it may be harmful in lepromatous cases. The following results were obtained from this treatment during 1943 —

Cases	Symptoms Disappeared	Improved	Stationary	Worse
2,328	114	223	1,763	85

The author does not claim that the treatment is a panacea for leprosy but he considers that the essence of citronella in his experience, is comparable in its effects with those produced by chaulmoogra oils. *L. Rogers*

ISWARIAH V. Acute Leprosy Reaction in Course of Thyroid Medication for Obesity *J Indian Med Ass* 1944 Dec. v 14 No 3 58.

LINHARES, H. Estudo sobre a célula leprosa do rato [Study of the Leprosy Cell in the Rat.] *Mém Inst Oswaldo Cruz*. 1944 Apr. v 40 No 2, 183-9 [17 refs.] English summary

As long ago as 1921 Gujo found that carmine and trypan blue when injected were taken up by leprosy cells. The author has now studied these cells and their staining affinities. He took eleven infected rats and divided them into two lots. Five were injected with lithium carmine freshly prepared, at 2-3-day intervals on four occasions: first 1 cc subcutaneously the next two 0.5 cc. intraperitoneally and lastly 0.3 cc. intracardially. The remaining six received injections of 1 per cent. trypan blue subcutaneously intraperitoneally and intracardially. The animals were killed at intervals and sections of the tissues stained. It was observed that the cells containing the bacilli were the ones which took on the stain, that these were reticulo-endothelial cells, histiocytes, and the stages could be seen of these cells becoming transformed into the typical leprosy cells. *H. Harold Scott.*

LINHARES H Possibilidades de transmissão e vias de inoculação da lepra murina em ratos e outros animais. [Possible Ways of Transmission of Murine Leprosy in Rats and Other Animals.] *Mem Inst Oswaldo Cruz* 1943 June v 38 No 3 321-51 [101 refs] English summary

There is little original work recorded in this article. It is a well-documented summary of evidence reported in the literature regarding the various points considered. A study of murine leprosy is important on account of the similarity between the lesions caused by it in animals and those found in human infection by *Mycobacterium leprae*. The author first reviews the evidence for transmission by insects considering *Lucilia caesar*, *Calliphora vomitoria*, *Musca domestica*, *Haematopinus spinulosa*, *Culex echidninus* and others. Though *Polypox spinulosa* was found to contain many bacilli after feeding on an infected animal no growth was obtained when these were planted on Löwenstein's medium. Rats were readily infected by feeding on diseased animals and also by contact the organisms entering by way of a skin lesion. Congenital transmission is not proven. The evidence for nasal instillation is conflicting as is that by intradermal inoculation. Intracardiac inoculation produced cutaneous and glandular lesions and later generalization. The opossum, *Didelphys aurita* was the species used and was found to be susceptible and responded to inoculation by subcutaneous injection in particular but also by the intraperitoneal, pleural and osseous routes. Chickens and pigeons were also infectible intramuscularly and the former intraperitoneally and *per os* the latter intravenously.

H Harold Scott

HELMINTHIASIS

GORSSE P & ACCART R. Essai sur le traitement de la bilharziose vésicale. [The Treatment of Urinary Schistosomiasis.] *Bull Inst Hyg Maroc* 1943 v 3 5-57 [48 refs]

This study of the treatment of urinary schistosomiasis was made on 65 recently infested European patients and 147 Africans in Morocco, most if not all, were soldiers. Owing to the exigencies of the war a few only of the cases could be followed up. After reviewing briefly the life-history of the parasite and the clinical course of the disease in man, with particular regard to its chronicity and relapses, the authors consider the tests by which the therapeutic effect of treatment with drugs may be judged. These tests are classified in four groups: (1) clinical signs—haematuria, cystitis, spermatozoospermia and fistula; (2) the presence and appearance of the ova in the urine; (3) the blood picture—eosinophilia and anaemia, and serological reactions (complement fixation and intradermal tests); (4) the results of cystoscopy. They conclude that cystoscopy gives the best test. The cystoscopic picture shows four distinguishable conditions representing stages in the course of the disease, but the authors admit that the bladder may show more than one stage at the same time. It is important to allow a sufficient interval between the end of a course of treatment and a cystoscopic examination.

In discussing treatment the authors mention electrocoagulation as a useful measure in certain cases, but it is reserved for the specialist and does not enter into the general treatment of the disease. Certain drugs—neocarphenamine, bismuth and emetine—have been proved to be useless, yet they are still included in textbooks. Antimony is the only parasiticide which they have used in this study, and they limit their observations to three preparations—tartar emetic,

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Fouadim, and antihiomaline. All these produced a good immediate result but as time went on a less favourable impression was produced particularly in the case of tartar emetic. In 57 cases treated by the authors with at least 1.60 gm. of the drug in four only was no immediate clinical effect seen, but when cystoscopy was used on 19 patients after two months eight were improved, seven were in the intermediate stage (eggs present) and four were not improved after four months there were four relapses two unchanged and two improved. No definite cure has been obtained.

Fouadim (sodium antimony pyrocatechun disulphonate) though easy to administer and free from toxic effects than tartar emetic was also disappointing they obtained no cure in 11 cases treated and abandoned its use. Antihiomaline in their opinion is the best of the three drugs but it is not a sterilizing drug in eight cases which they were able to review later there were four relapses.

The authors state that antimony is not a specific for schistosomiasis like mercury in syphilis it is insufficient by itself and what is needed is to find a series [generic] of parasitocidal compounds to be given together or in succession.

J F Corson

SANABRIA, A. Syndrome de Stokes-Adams por miocarditis bulhariana. [The Stokes-Adams Syndrome due to Bulharian Myocarditis.] *Rev Polidica* Caracas 1944 July-Aug. v 13 No 77 282-83 3 figs. [34 refs]

A free translation of the author's summary reads as follows —

Two patients were admitted to hospital with the Stokes-Adams syndrome in whom clinical, radiological, electrocardiographic and laboratory examinations showed the presence of bulharian myocarditis. In the first patient the electrocardiograph revealed auricular fibrillation complete A-V block, intraventricular block and ventricular extra-systoles. While the electrocardiogram was being taken the patient fainted and there was transitory ventricular fibrillation. In the second patient there was bulharian myocarditis but the mechanism of the syncope attacks was not clear.

WITTEBERG G. What is the Cause of the Parasitic Laryngo-Pharyngitis in the Near East ("Haloun")? *Acta Med Orientalis (Palestine & Near East Med J)* 1944 Nov-Dec. v 3 No 6 191-2

The word *Haloun* means snail but it is applied to other bodies with a coiled appearance. In the Near East in Lebanon and Syria, a leech *Limnatis nilotica* and a fluke *Clinostoma complanatum* are found in the throat of man. The former occurs in water and is taken in by man when drinking such water. The fluke may harbour as many as 30 at a time man as a rule one only. The latter the fluke is about half an inch in length is parasitic commonly in fish-eating birds and is acquired by man through his eating insufficiently cooked fish infested with the metacercariae of the fluke. Once before a case of human infestation by *Clinostoma complanatum* has been recorded, namely by J YAMASHITA in 1938 (*Ann Zool Japonenses* v 17 563).

Fasciola hepatica has also been incriminated as a cause of *Haloun* but on insufficient grounds.

GIBSON T E. Tapeworm in Freshwater Fish. [Correspondence] *Brit. Med J* 1945 Feb. 10 199-200.

The author reports a very mild outbreak of tapeworm infestation of trout in a reservoir in Northamptonshire which occurred in August and September 1944. Thirty nine plerocercoids were recovered from the peritoneal cavity of one of the

affected trout and were fed to 1 guineapig and 3 rats the guineapig showed no signs of infection but all the rats passed eggs of *Diphyllobothrium* in their faeces and finally recovered spontaneously. At the time when the trout were dying 50 grebe [aquatic birds] also died but it is not known whether they were infected with *Diphyllobothrium*. Later over 100 smaller fish were caught in this réservoir and 40 per cent of them were found infected with plerocercoids of a smaller type than those recovered from the trout. Attempts to infect rats with these were not successful.

J. F. Corson

UNSWORTH K. Observations on the Life-Cycle of a Species of *Diphyllobothrium* found Parasitizing Trout in Great Britain. *Ann Trop Med & Parasit* 1944 Dec 30 v 38 Nos 3 & 4 213-19

This is an account of Unsworth's work on the life-history of the *Diphyllobothrium* tapeworm the plerocercoids of which were discovered by DUGUID and SHEPPARD [this *Bulletin* 1944 v 41 857] in trout and sticklebacks in a South Wales reservoir. Beginning with an infested rat sent to him by Duguid and Sheppard Unsworth infested as Duguid and Sheppard did the copepods *Diaptomus gracilis* and *Cyclops strenuus* finding that the latter was the more efficient first intermediate host and easier to maintain in the laboratory. He describes the developmental stages in these crustacea. After 16-20 days development of the larvae in *Cyclops* 34 sticklebacks were fed with the infested *Cyclops* and 22 of them became infested with plerocercoids situated chiefly on the serous surface of the stomach under the peritoneum and under the liver capsule. Some infested sticklebacks were fed to a single pike in which a single plerocercoid developed. Plerocercoids from both the infested sticklebacks and the pike were fed to puppies aged 2-3½ months and the adult tapeworm developed in the puppies which passed eggs in their faeces. Coracidia from these eggs infested *Cyclops*.

Unsworth makes the epidemiologically important suggestion that the trout in the South Wales reservoir became so heavily infested (100 per cent) in so large an expanse of water because they ate infested sticklebacks. He points out that the commoner fish hosts of plerocercoids of *Diphyllobothrium* species (e.g. pike perch wall-eyed pike trout burbot) eat other fish while the less common fish hosts (e.g. grayling pollan) eat other fish only at times.

Unsworth also received from HICKEY plerocercoids of the *Diphyllobothrium* species found by HICKEY and HARRIS [this *Bulletin* 1944 v 41 858] in the Dublin area and found that these also developed to maturity in puppies. Since Hickey and Harris found adult *Diphyllobothrium* tapeworms in gulls and cormorants this species can apparently develop in both a bird and a mammal. Unsworth could not identify the South Wales species because he recovered from the puppies only the scolex and some immature anterior segments but he concluded that this species was too small to be *D. latum* which infests man. Unsworth also concluded that the Dublin species was certainly not *D. latum*. There is no proof he thinks that the Dublin and the South Wales species are the same.

All these workers have submitted specimens of the adult tapeworms obtained by them to H. A. BAYLIS of the British Museum and BAYLIS [this *Bulletin* 1945 v 42 302] reports that all the tapeworms obtained from the gulls represent one species and all those obtained from the cormorants another. Comparison of the worms obtained from the experimental mammalian hosts by all the workers led Baylis to conclude that all the workers were dealing experimentally with a single species which is probably *D. dendriticum* (Nitzsch 1824) which is normally a parasite of gulls. This decision seems to rule out the possibility hinted at by *The Lancet* [1944 April 8 475] that the South Wales

species might be *D. latum* which might be introduced into Britain by refugees from Norway or Poland, as it has been introduced into North America by immigrants and has become endemic there. [The relationship between *D. latum* and the Diphylobothriid tapeworms of birds needs further study in this country. The larval stages of both occur in copepods and fish and are morphologically similar. There are other recent records of these larval stages in fish. Thus Duguid and Sheppard (*loc cit*) state that Dr PETERSON of Yell informed them that a species of *Diphylobothrium* is endemic in trout in some of the Shetland Islands and GIBSON [above] records infestation of trout in a Northamptonshire reservoir with plerocercoids morphologically similar to those described by Duguid and Sheppard (*cf* also T HARE *Brit Med J* 1945 Mar 10 347).

With regard to the infestation of man with *D. latum* in west Ireland O'CONNOR [this Bulletin 1945 v 42, 218] discussing multiple infestation of man with this species states that the first case of multiple infestation was recorded by O'FARRELL (*Irish J Med Sci* 1930 vi 542). ANDREWS and OLIVER (*Brit Med J* 1944 June 3 772) record a case of multiple infestation with *Taenia saginata*.
G. Lapage

MAZZOTTI L. Observaciones en 10 individuos parasitados con *Taenia saginata*. Presencia de huevecillos en la región perianal y en otras regiones cutáneas. [Observations on Ten Individuals Infested with *Taenia saginata*. Presence of Eggs in the Perianal Region and other Cutaneous Areas.] *Rev Inst Salubridad y Enfermedades Trop Mexico* 1944 Sept. v 5 No 3 207-13. English summary (8 lines).

The ten individuals examined came from different classes of society. The methods of examination used were (1) Examination of the perianal region by Graham's adhesive cellulose tape [see comparison of this method and HALL's NIH swab for the diagnosis of enterobians MAZZOTTI and OMORIO this Bulletin 1943 v 40 617 and description of the NIH and GRAHAM's swabs, this Bulletin 1942, v 39 780]. The author had previously (*Rev Inst Salubridad y Enferm. Trop* 1944 v 5 153) found eggs in the perianal region of 15 individuals infested with *Taenia saginata* and of one infested with *T. solium*. (2) Faecal examination by direct smear which by itself would the author concludes have given a much lower percentage of positives. When direct smears were negative (aecae were also examined by the TELEMANN RIVAS centrifugation method and, in some instances by the STOLL method [this Bulletin 1923 v 20 950]).

The results were. Out of 106 examinations of the perianal region of the ten individuals 92 (85 per cent) were positive. It should be noted that while nine of the patients were given only 4-9 daily examinations with varying results one patient (No. 26) was given 41 daily examinations all of which were positive. The same observation applies also to the 131 examinations of 61 faecal samples from the ten patients of which 96 (73 per cent) were positive. Here again patient No. 26 supplied 22 samples of which 58 examinations were done 86.2 per cent. of them being positive.

Other regions of the skin of three of the patients were examined by the Graham method, five eggs being found in the lumbar region of one patient, nine in the hypogastric region of another and 181 between the neck and knees of the third. Eggs were also found on the underclothes of some patients.

The author thinks that the presence of the eggs in the perianal region and on the underclothes helps to explain self-infestation and infestation of others with cysticerci of *T. solium*. He thinks that while most reports of self-infestation with cysticerci of *T. saginata* are doubtful some are proven (*cf* g

FONTAN *Gaz de Hôp* 1919 v 92 183 and DE RIVAS D 1937 cited by FAUST *Human Helminthology* 2nd Ed. 1939 p 314) and may be explained in the same way

Mazzotti found that proglottids of *T. saginata* placed in a Petri dish immediately after they had been passed expelled from their extreme anterior ends after a few seconds or minutes a milky fluid full of eggs. He calculated that each expels an average of 97 080 eggs. In stained and sectioned proglottids he noted that the branches of the uterus do not stop at a certain distance from the anterior border as most textbooks say but actually reach this border so that when the proglottid is detached these uterine branches actually communicate with the exterior. Through them the eggs are expelled. The posterior uterine branches do not reach the posterior border. The disintegration of the proglottid is therefore not necessary for the expulsion of the eggs. The proglottid is in fact an organism which actively expels the eggs by its contractions as it crawls about the pressure of the anal sphincter which the author suggested in an earlier paper as one cause of expulsion of eggs in the perianal region is not necessary.

[PODYAPOLSKAYA V P (this *Bulletin* 1944 v 41 301) refers to the wide use in Russia of the method of scraping the perianal folds for the diagnosis of enterobiasis he also recommends it for the diagnosis of infestations with *T. saginata*. Podyapolskaya quotes the work of SHITOM S K who also noted that proglottids of *T. saginata* crawling in a Petri dish extrude eggs by channels opening at the anterior border and leave behind a milky fluid full of eggs extruded as a result of the contractions while crawling. G Lapage.

BARNETT L. Colossal Hydatids associated with Choleperitonaeum. *Med J Australia* 1944 Nov 11 v 2 No 20 511-14 7 figs

This is the follow up story of the case described in this journal on December 24 1927 at page 878 [this *Bulletin* 1928 v 25 461]. The patient now aged 55 years fell forward on to a large stone when he was six years old [in 1895 ?] and must have caused a hydatid cyst of the liver to burst into the peritoneal cavity. After being acutely ill for three weeks he gradually recovered but after two or three years his abdomen was seen to be becoming more prominent and this slow increase in size continued for the next 30 years. It was always diagnosed as ascites probably tuberculous and attempts at aspiration failed. An operation was declined because the patient said he felt strong and fit to work. Finally his health deteriorated and he was sent to the author in February 1927 he was then gravely ill and had an enormously distended abdomen measuring 57 inches in circumference while his weight was 17 stone. Thinking that he had ascites possibly purulent the author inserted a fine trocar without result then a larger one (1 mm.) still without escape of fluid and finally a 2mm. trocar produced unmistakable shreds of hydatid cyst which were further identified by microscopical examination. The Casoni and R.C.F. tests were positive but eosinophilia was only 2 per cent.

Operation was performed on February 24th, 1927 and daughter cysts, varying in size from cherries to coconuts were evacuated filling bucket after bucket until 50 litres (11 gallons) at least were removed. The abdominal viscera were all matted and crowded behind a false membrane about 3 mm. thick. The wound healed in 10 weeks and the patient then weighing 12 stone was able to resume his work as a shepherd.

After three or four years two cysts were observed growing in the lower part of the abdomen but the patient refused operation for 16 years being then

aged 35 The second operation was performed on September 5th, 1943 the two cysts about the size of foetal heads were opened and drained and the patient was discharged well on November 23rd, 1943

At the second operation the peritoneum was found to have returned to its normal state as regards its structure and relation to the viscera. Another point of interest is that the two cysts had taken 16 years to grow to the size of foetal heads.

J F Corson

- i. LANE C. Threadworm Infections, Prevalence, Pathogenicity Periodicity and Prevention. *Lancet* 1944 Oct 14 511-13 [32 refs]
- ii. PAKENHAM WALSH R. Threadworm Infections. [Correspondence] *Ibid* Nov 4 612

i. Clayton Lane has here brought together a large body of information about *Enterobius* and shows that there is still much that is unknown. For instance the events in its life-history between entry into the nose or mouth and arrival in the rectum remain a subject for speculation. Infection is very widespread, as investigations in the United States and Britain have recently shown, but the curious fact that American Negroes show lower infection rates than the white race is somewhat puzzling.

The pathogenicity of this worm is debated, especially in relation to the appendix. The fact that it and its eggs have been found in abscesses about the rectum is explained by Lane as a sign that it will travel to seek conditions suitable for oviposition (usually on the skin outside the anus) and that it will oviposit wherever those conditions are favourable. Lane sees a nightly periodicity in its habit of parturition similar to that of the periodic race of *Trichinella brevicornis* and promises further evidence based on examination of the studies of Professor F W O Corvax.

Prevention of infection is shown to be difficult especially in regard to air borne infection. It will probably be a matter of treatment on a large scale at the ideal drug has yet to be found. The infection is usually trivial, and of the no drugs mentioned gentian violet may cause intestinal irritation and phenothiazine may be dangerous. No drug is yet known that is deadly to the worm yet less risky to man than is the infection. It needs finding.

ii. Pakenham-Walsh has used methylene blue (grains 3 t.d.s. for a week) with apparent success in two adults.

Charles H Walcotts

PICOURY L. A propos d'une epidemie de trichinose à Beyrouth (Liban) [Concerning an "Epidemic" of Trichinosis at Beyrouth, Lebanon.] *Bull. Soc Path Exot* 1943 Mar 10 and Apr 14 v 36 Nos. 3-4 88-94

The occurrence of human trichinosis at Beyrouth between December 1939 and March 1940 was reported by B SAAD (*Presse medicale* 1940 v 48 p. 556) and by P MILLISCHER and Y DELBARRY (*Biologie medicale* 1942, v 32 23). Discussing this outbreak Picoury recalls that WORTABET (cited by E. BRUMPT *Précis de Parasitologie* 1936 5th ed p 1055 without reference and mentioned also by STRONG R P STITT's *Tropical Diseases* 6th ed 1942 p 1241)) recorded Trichinella fifty years ago [Brumpt in the 5th ed gives no date] in a boar in Southern Lebanon. This suggests infestation of the wild fauna of this district especially the rat which is very abundant there.

In 1840 the Army Veterinary Laboratory found that a notable proportion " [no figures given] of rats of Beyrouth were infested. It is unlikely that trichinosis died out after Wortabet a record of it. It was probably not recorded because rats and pigs were not examined and no human case was suspected. Human infestations may however be latent and there may be no symptoms in

the rat or in even well fattened pigs harbouring a heavy infestation. The most important reason why trichiniasis may not have been recognized in Lebanon is however the small consumption of pork there. Before the French occupation practically no pigs were reared and even after it they were reared only for the needs of Europeans and some Lebanese Christian families. For the last ten years only about 2 000 head were consumed annually which allows hardly six pigs a day for a million people. Pig rearing is practically confined to the Beyrouth district.

Only a few human cases were recorded in the 1939-1940 outbreak. [No figures are cited.] These cases were not confirmed by biopsy or by skin or serological tests. Rumour magnified the extent of the outbreak and there was a considerable decrease in the demand for pork. The authorities under the impression that pigs infested themselves by eating faeces of infested animals ordered the slaughter of pigs wherever *Trichinella* was found and of all the pigs at one piggery at Beyrouth which was situated near an abattoir and a refuse depot the pigs being fed almost entirely on waste from the abattoir and on material from the refuse depot which contained carcasses of dead rats. This amounted to a veritable experimental infestation of these pigs. During the mass slaughter at this piggery between January and March the Army Veterinary Laboratory recorded that 15 per cent of about a thousand pigs examined were infested. The trichinized meat was destroyed by the authorities but carcasses not condemned were allowed to go to market at a time when fear of infestation has greatly reduced the demand for pork so that great waste occurred at a time when wartime feeding of the people was difficult. Later the Army Veterinary Laboratory was required to examine all carcasses with the following results. May to December 1940 in Beyrouth and district 1 234 pigs were examined and 16 were positive (1.3 per cent). January to September 1941 (when the French evacuated the Levant States) 1,273 pigs were examined in the same area and seven were positive (0.54 per cent).

These figures represent Pigouy thinks the average infestation better than the 15 per cent. recorded from the Beyrouth piggery mentioned above. The infestation of pigs was thus moderate. The author quotes the following percentage infestation of pigs in other countries. Germany 0.05 to 0.1 Bulgaria 3.2 [cf BRUMPT also 5th ed. p. 1 055] Rumania 0.15 America 4.5 and 8 [CRAIG and FAUST *Clinical Parasitology* 3rd ed. 1943 238 quote RANSOM's (1916) estimate that 6 per cent. of American hogs are positive]. In some Lebanese piggeries 30, 60 and 100 kilometres from Beyrouth including Damascus and Aleppo no *Trichinella* were found, but the number of examinations was admitted to be quite insufficient. Thus trichiniasis in Lebanon seems to be confined to the Beyrouth district to which pig-rearing was at the time of writing also confined but if pig rearing spreads elsewhere trichiniasis will probably spread with it.

Sarcocystis was found in 30-40 per cent of the pigs examined. [The remarkably good results of the assumption by the Royal Army Veterinary Corps of responsibility for meat inspection and also for administration of livestock depots and the rearing of animals for the supply of meat to Allied armies throughout the Middle East (see *Vet Rec* 1944 Nov. 18 447 and *Nature* 1945 Jan. 13 60) must have altered the situation considerably since the French evacuation of the Levant.]

G. Lapage

MONNIG H. O. Trichinosis in South Africa. *South African Med J* 1944 Dec. 23 v. 18 No. 24 420

Trichiniasis has never been found in domestic animals in the Union of South Africa as however the methods of examination were formerly inadequate to

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show light infestations the authors used the digestive method. Pieces of the diaphragm muscle of pigs (about 5 gm. from each pig) were cut up and digested for 24 hours or longer at 37°C in 300 cc. of normal saline containing 0.15 gm. of papain per 100 gm. of muscle. The liquid was then poured into a funnel provided with a wire gauze diaphragm covered with cheese cloth. After a few hours a few drops from the bottom of the funnel were drawn off and examined.

During four months 1,352 pigs were examined in this way with negative results. As the pigs came from a large area of the country they were regarded as representative of the greater part of the Union and it was concluded that trichiniasis must be absent or very rare in the Union. This view is supported by the fact that raw pork is very rarely given to pigs in South Africa.

J F Carson

SPRUE.

FREED, E. D. & MATER, D. A. Intrahepatic Obstructive Jaundice following Mapharsen, with Development of a Sprue-like Syndrome. *J Amer Med Ass.* 1944 Dec 2, v 126 No 14 882-4 1 fig.

The case recorded in this communication resembles others in a series of cases of postarsphenamine icterus published by HANGER and GUTMAN (*J Clin. Invest.* 1939 v 18, 281). *J Amer Med Ass* 1940 v 115 263). A negro aged 27 who was found to have positive Kahn and Wassermann reactions was treated with Mapharsen and a bismuth compound after the third injection jaundice developed and gradually became more intense.

As laboratory tests pointed to obstructive jaundice a laparotomy was undertaken 33 days after admission to hospital, but no obstruction was under a biopsy of the liver taken at this time showed distension and plugging of the canaliculi, with biliary thrombi. The syndrome of obstructive jaundice was evidenced by a steadily deepening icterus with clay-coloured stools without enlargement of liver or spleen with negative urms urobilinogen, immediate direct van den Bergh reaction, elevated serum cholesterol, negative cephalin cholesterol test, no increase of prothrombin time, adequate excretion of hippuric acid and normal serum protein partition.

But after the laparotomy it became evident that this was an example of intrahepatic post-arsenical obstruction as originally described by Hanger and Gutman. The prolonged clinical course and the onset with erythema and fever following the third injection of an arsenical were identical with the syndrome described. A sprue-like syndrome supervened during the gradual disappearance of the jaundice. Thus the previously normal glucose tolerance curve became flat and this abnormality could be ascribed to faulty absorption by the intestinal tract.

The probability that such a deficiency existed was emphasized by the appearance of voluminous greasy stools containing large amounts of fat during the time that the bile was reaching the intestine as well as by the low figure of the blood calcium.

The demonstration of tryptem and lipase in the duodenal contents suggests that the steatorrhea was not due to deficiency of pancreatic enzymes.

It is of interest to note that a similar intrahepatic lesion has been observed in some cases of steatorrhea in infants.

P Manson-Baker

HAEMATOLOGY

SINGH B Nutritional Macrocytic Anaemia amongst Vegetarians in Forward Areas in the Middle East Campaign *Indian Med Gaz.* 1944 Nov v 79 No 11 531-5

Five cases of macrocytic anaemia occurring in vegetarian Indian soldiers in the Persia and Irak Force were studied by the author

The initial red-cell counts ranged from 1.40 to 1.75 millions per c.mm. the colour indices from 1.0 to 1.2 and the mean-cell diameters from 7.6μ to 7.8μ [technique not stated] Normoblasts were present in all the cases [presumably in the peripheral blood] while megaloblasts were seen in only one case

In three of the patients the gastric juice was examined and found to contain free hydrochloric acid Laboratory examinations for malaria and worm infestation were negative throughout The van den Bergh test was also stated to be negative. The sternal marrow was apparently not investigated.

The clinical manifestations were those of anaemia in general no special signs of nutritional deficiency being noted. The ages of the patients are not mentioned but it is noted that three of them were soldiers of ten years' service

The response to treatment is difficult to analyse from the data presented since it is evident that in all five cases admission to hospital was followed by vigorous blood regeneration. No details are given of the diets received by the patients Two of them were treated with iron supplemented by a single blood transfusion one of these also received oral liver extract for four days. The other three patients were given oral or parenteral liver extracts over varying periods Examination of the protocols however provides little reason for believing that the liver therapy played an essential part in maintaining the subsequent haematopoiesis

The author points out that the patients, of whom three were Rajputs and two Jats came from communities whose staple diets of fresh milk and ghee normally provide important sources of vitamins whereas on active service this was replaced by dried or evaporated milk which is likely to result in impaired vitamin intake He concludes that the cases of anaemia under consideration probably resulted from dietary deficiency but whether the deficient factors were primarily proteins or vitamins could not be established.

[Such examples of severe anaemia presumably nutritional in origin provide enviable opportunities of advancing our understanding of the fundamental causes of defective haematopoiesis The attainment of this object however calls for the application of modern haematological methods in conjunction with planned therapeutic trials.]

L J Davis.

VENOMS AND ANTIVENENES

POPE C H & PERKINS R M Differences in the Patterns of Bites of Venomous and of Harmless Snakes. *Arch Surgery* 1944 Nov v 49 No. 5 331-6 8 figs

The authors performed experiments with *Crotalus atrox*, *Ancistrodon piscivorus* and *A. mokasen* making the snakes bite plasticine and plastic cylinders approximately the size of the human wrist and a gelatin cast of a hand.

They conclude that the reptiles bite and do not stab Under the conditions of the experiments the objects bitten were marked by the teeth of both upper and lower jaws.

B G Macgrath

SERGEANT Et. Action d'un sérum préparé avec du venin de vipéridés du genre *Cerastes* sur l'envenimement dû aux vipéridés du genre *Vipera* [The Action of Anti-*Cerastes* Serum in Poisoning by Snakes of the Genus *Vipera*] *Arch Inst Pasteur d'Algérie* 1944 Mar v 22 No. 1 16-17

The Viperidae of Algeria are of the genera *Cerastes* (*C. cornutus* and *C. vipera*) and *Vipera* (*V. lebetina* and *V. ammodytes*)

The antivenene prepared against snakes of the genus *Cerastes* will cure 90 per cent. of animals given a lethal dose of the homologous venoms but will also cure 65 per cent. of those given a lethal dose of the venom of *V. lebetina*. The practical conclusion is that if the proper antivenene against *Vipera* species is not available for a person bitten by those snakes the *Cerastes* antivenene may be used with some prospect of success.

Charles Wilcocks.

WILLIAMS E. R. & DAVIES A. B. A Case of Alder Bite [Memoranda.] *Brit. Med. J.* 1945 Feb. 17 223.

SERGEANT Et. Sérothérapie antiscorpionique (septième note) Observations médicales reçues pendant l'année 1943 [Anti-Scorpionale Serotherapy Seventh Note 1944.] *Arch Inst Pasteur d'Algérie* 1944 Mar v 22 No. 1 18-30

The scorpion has been identified during 1943 in only 58 of 390 recorded cases of scorpion sting — *Priocryptus australis* 48 *P. amoenus* 1 *P. hopperensis* 1 *P. howilli* 3 and *Buthus occitanus* 3. In that year the condition of 104 of these patients was classified as grave (24 being almost in extremis). 78.8 per cent. of these were cured by antivenene injection. Since 1936 83.5 per cent. of 1,428 persons in a grave condition from scorpion sting have recovered after having received antivenene. Of those who succumbed in spite of antivenene, it is known that more than half either received insufficient dose or were treated too late.

Charles Wilcocks

SERGEANT Et. Sérothérapie antiscorpionique de l'emploi du sérum anti scorpionique en injection rectale contre l'envenimement scorpionique. [Scorpion Antivenens per rectum] *Arch Inst Pasteur d'Algérie* 1944 Sept v 22 No. 3 177-8

Scorpion antivenene injected per rectum has no curative action after scorpion sting. Rectal saline injection does not reinforce the action of antivenene.

Charles Wilcocks

SMITHERS R. H. N. Contributions to our Knowledge of the Genus *Latrodectus* (Araneae) in South Africa. *Ann. S. Afr. Mus.* Cape Town 1944 v 38 Pt. 3 263-313 1 pl. 2 folding maps & 20 figs. [79 refs.] [Summary taken from *Rev. Appl. Entom.* Ser. B 1945 Jan v 33 Pt. 1 12]

Most of the cases of illness or death due to the bite of females of *Latrodectus indistinctus* P. Camb. in South Africa occur during the harvest season in the grain lands of the coastal belt of the Western Province. During this season, when the spiders are particularly numerous, reaping operations destroy or expose their nests and they build new ones under the sheaves lying on the stubble to dry. The men who stack these collect several under their arms and so may disturb the spiders and cause them to bite. During the 1936 harvest a survey of a considerable area showed that one of every six sheaves had a nest on the underside. A detailed account is given of the bionomics of this spider.

including the method of building the nest mating and depositing the eggs and the development of the young within the egg-sacs and their dispersal with short notes on *L. geometricus* Koch which has only once been recorded as causing illness by its bite and has a much less potent venom than *L. indistinctus*. It is considered likely that both species occur throughout South Africa their known distribution there is shown on maps.

The author also describes both sexes of *L. geometricus* and *L. indistinctus* discusses and figures the abdominal pattern of the immature stages of the latter and distinguishes a new variety *L. indistinctus* var *karrooensis* which appears to occur only in the high parts of the Karroo on the basis of differences in abdominal pattern and coloration in the adults and differences in the nests and webs. He considers that *L. concinnus* P Camb is a synonym of *L. geometricus* since examination of the types showed that they agreed in every respect but darkness of colour and every variation from pale grey to black has been found in the field.

SERGEANT Et Essais de sérums antivenimeux contre le venin d'abeille. [Trials of Antivenenes in Bee Stings.] *Arch Inst. Pasteur d'Algérie* 1944 Sept. v 22 No 3 175-6

Neither scorpion antivenene nor a serum prepared against *Cerastes* is active against bee venom.
Charles H ilcox

TROPICAL ULCER

PROC ANN GENERAL MEETING OF ASSAM & NORTHERN BENGAL BRANCH BRIT MED ASS SHILLONG 4th-7th NOVEMBER 1943 42-7 1944 Calcutta. Indian Tea Association Discussion on the Epidemiology and Treatment of Naga Sore. [LEWIS J A LAPPING BURKE MCCOMBIE SHORTT JELLISON & others]

In this discussion of Naga sore (which is presumably the same as tropical ulcer see this *Bulletin* 1944 v 41 614) the impression given by several speakers is of the great importance of the infective element in the epidemiology of this disease. Lewis Lapping and others give instances of labourers returning from work in other areas to tea gardens in which Naga sore was not at the time prevalent and of the occurrence of other cases in the tea garden population shortly after the introduction of the infection to the community. McCombie refers to hospital transmission in which a compounder transmitted the infection to a simple cut and Choudhury mentions multiple sores in which presumably the discharges from one infect the skin elsewhere. The importance of initial trauma is recognized but Lewis remarks that the contact cases he has seen were in persons of poor physique and malnourished. Lapping remarks that we know no more at the present time than was apparent 30 years ago. He also thinks that malnutrition especially of the skin with its terminal blood supply is a factor and assumes that the infective agent is the anaerobic fusiform bacillus.

Charles Wilcocks

PATTANAYAK G C Tropical Ulcer in Angul, Orissa *Indian Med Gaz* 1944 Nov v 79 No 11 521-6 1 chart

Cases of tropical ulcer were rare if present at all in Angul until recently when they began to appear in labourers introduced from Assam. Since May

[May 1945]

1942, when the author saw his first case the number rose to a peak in August-September then a steady decline set in for the ensuing 7-8 months. Of 90 cases the subject of this study all but two were males (but the relative numbers at risk are not stated). The poorer and lower social groups were mostly attacked those higher in the social scale under very similar conditions largely escaped. As usually observed, the ulcers were commonest on the legs in those debilitated from malnutrition, malaria hookworm etc and started in some local trauma which became infected. Organisms found were very varied and numerous staphylococci streptococci Vincent's spiroillum *Fusiformis* *fusiformis* and diphtheroids (never the true Klebs-Loeffler organism as in Yeldt sore) If left untreated they were very indolent and slow to heal. Various forms of treatment were tried but no specific cure was found. Sulphapyridine applied locally got rid of the organisms but seemed to retard rather than to hasten healing moreover sulphamylamide which was cheaper gave equally good results. NAB Neocarphenamine was not effectual. In the indolent stage copper sulphate proved useful as did 2 per cent perchloride of mercury ointment but not in the final healing stage. In short sulphamylamides in the earlier stages applied locally (not internally) and copper sulphate later gave the best results. Potassium permanganate and acriflavine proved useless in any stage.

IRVING C. Treatment of Ulcers by Plaster Casts. [Memoranda] Brit Med J 1945 Jan 27 120

The author writes from the Meru district of Kenya where the standard of living is very poor the people heavily infected with yaws and the incidence of ulcer high. Food shortages periodically lead to outbreaks of ulcers some of which approximate to a nutritional type others are simply yaws and no doubt many are of mixed type. No attempt was made to differentiate these nor was it necessary because they were equally intractable to the usual local treatments (resol, fomentos cod liver oil elastoplast copper sulphate carbolic) and reacted equally well to plaster of Paris. All patients received arspenamine and butemth injections a good diet towns and treatment for worms (if required). Local treatment consisted of cleaning or scraping the ulcer application of powdered sulphamylamide in some cases covering with lint on which Zipp [this Bulletin 1944 : 41 77] has been smeared, and enclosing in plaster. As a rule in two or three weeks the plaster could be removed when it was found that the ulcer had become lean although had separated and the area was ready for grafting. A very striking change was noticed in the patients within two or three days of the application of plaster the pain was relieved, the temperature fell and the mental attitude changed from despair to cheerfulness. [GURDLEY this Bulletin 1944 : 41 777] also advocates plaster in the treatment of tropical ulcer.]

Charles W. Weeks

MISCELLANEOUS DISEASES

INDIA. Proceedings of the Conference of the Medical Specialists Central Command and North Western Army and of the Joint Meeting with the Civil Medical Officers Punjab held at Lahore in February 1944 150 pp. 1944 Allahabad Supt Printing and Stationery United Provinces.

This is a report of the proceedings of a Conference at which about 75 Army medical specialists were present. It contains more than 150 pages of closely

printed matter most of which is of great interest and importance. An adequate summary within a reasonable compass is quite out of the question. The conference must have been of immense value to all who were present and the report deserves the widest circulation among medical officers in India and the Far East.

Anaemia and Malnutrition were dealt with as a single subject and no less than 17 of the specialists took part in the discussion. It was generally agreed that malnutrition constituted the basic condition in which malaria, the dysenteries and hookworm disease readily caused the three main types of anaemia so prevalent among the Indian troops. Deficiency of the Wills factor in the diet caused the macrocytic nutritional anaemia which appeared to be the same as the macrocytic anaemia of pregnancy. Deficiency of iron caused microcytic anaemia and deficiency of both these factors caused the combined or dimorphic anaemia. In many cases defective absorption of these factors seemed to play the chief part so that large doses of crude liver extracts of the campolone type or large doses of ferrous sulphate by mouth or combined treatment by both of these drugs had to be given. But even with adequate specific treatment of these kinds there were many failures which were attributed to keeping the patients on hospital diets. One speaker had obtained a startling degree of improvement in the results by opening a special kitchen in which voluntary workers, all of them Indian ladies, prepared tasty dishes containing the necessary articles of food, such as eggs, butter, milk, chicken, liver, fish and yeast. Several speakers advocated whole-blood transfusions for severe attacks; unfavourable results were mentioned but these were attributed to faulty technique. The great prevalence of the anaemias among Indian Other Ranks was attributed to the recruitment of many of these men from areas where malnutrition was prevalent but several speakers were critical of the rations supplied to the Indian troops. It was pointed out that the British soldiers in India suffered little from the anaemias probably because of the larger meat ration.

Diseases of the Typhus Group were discussed at considerable length and mention was made of the recent occurrence of a large number of outbreaks which were rather unhappily described by some speakers as endemic types. Most of the outbreaks appear to have been of the mite-borne and tick-borne types though there was a pronounced degree of reluctance to attribute particular outbreaks to individual vectors and there was evidence that occasional cases of flea-borne typhus occurred in many parts of India.

Some of the outbreaks were as follows —

(1) In Ranchi (Bihar) between 27-12-42 and 14-2-43 there were 35 cases among British troops doing field exercises in jungle country. Two of the patients were officers; these reported having been bitten by ticks; none of the other patients admitted having been bitten by any insects except mosquitoes. The agglutination reactions were of the indeterminate type.

(2) In and near Calcutta 156 cases were seen in 1942 and 1943 including an outbreak with 49 cases in two Indian regiments stationed at a village 80 miles from Calcutta; all these 49 cases were of the OXA type but no eschar was detected on any of the patients. Most of the other cases seen in Calcutta were also of the OXA type but a few were of the indeterminate and OXI9 types and some were negative to all three *Proteus* OX organisms.

(3) More than 300 cases occurred in the 14th Army on the Assam-Burma border during the last four months of 1943; all were of the OXA type and in 15 per cent of the British-Other Rank patients there was an eschar with lymphangitis. The case-fatality rate was about 7 per cent. A K strain of rickettsia was isolated from one patient. In this outbreak 130 cases occurred within a few weeks in two companies of a British battalion operating on the

slopes of a hill on which palm trees were growing. These were the only palm trees "for many miles around."

(4) A small outbreak, in which 11 cases occurred during November and December 1941 among troops doing jungle training near Bombay was of an exceptionally mild type. The agglutination response was of the OX2 type in six cases (maximum titre 1-1,250). It was negative in the others. The rash appeared at or soon after the onset. This outbreak was suspected of belonging to a special type.

(5) An outbreak of 11 cases was mentioned as having occurred at a Prisoner of War Camp at Bauragari (? locality) with a high mixed OX2 and OX19 rise in agglutinins in nine of the cases.

(6) The occurrence of about 400 cases of Q fever at Dehra Dun (United Provinces) in 1941-42, was mentioned by Lt-Col. PASTORCHA. The diagnosis was clinical, confirmed later by highly suggestive agglutinations done by Burnett in Australia. No further information is given of this remarkable outbreak.]

(7) In the Maldives Islands 214 cases of the OXA type were seen between May and December 1943. An eschar was seen in some of the cases.

(8) It was stated that quite a number of cases of tick typhus were seen in Arakan in 1943. There was a varying degree of agglutination of all three *Proteus* O V organisms. In two cases a hard tick was found on the patients.

(9) In 1943 there were 165 cases in the Central and Southern Commands "of all three endemic types."

(10) The only occurrence of louse-borne typhus recently reported in India was a mild outbreak in Peshawar City among the civilian population, in 1943.

The Dysenteries—The importance of immediate expert examination of perfectly fresh stools was stressed. Three speakers reported excellent results in bacillary dysentery from the use of sulphapyridine which was given when sulphaguanidine was not available. There was general agreement on the desirability of giving a generous diet as soon as possible. One speaker referred to "the pernicious use of salts" in treatment.

[This doctrine ought not to remain unchallenged. There is a general tendency among the younger physicians to regard the saline treatment as being discredited, and it is high time that carefully-controlled tests should be carried out before this time-honoured treatment is discarded. LEISHMAN and KELBELL have recently convinced themselves that "saline treatment has definite value." (This Bulletin 1944 v 41 1063). It was stated that Dr DAS GUPTA, Director of the Calcutta School of Tropical Medicine, had examined the stools of 300 "British Other Ranks" who had lived about one year in India [and who presumably were free from symptoms]. After a single examination the rate of infestation with *Eutamias histolytica* was found to be 28 per cent. (cysts only 17 per cent. cysts and vegetative forms 7 per cent. vegetative forms, alone 2 per cent.) This high rate was suspected to be due to contamination of the Calcutta water supply by sewage.

Tropical Eosinophilus—The association of this condition with asthma was mentioned as existing in a group of 12 cases. In six of these special enquiries were made regarding the residence of the patients, and it was found that only one had lived near the sea, the other five had lived near large rivers or canals. It was stated that Dr BRADSHAW of Bombay insisted on the need for a course of at least eight injections of "A.B." if relapses were to be prevented.

Malaria—Brigadier COVELL contributed a note on treatment. He was opposed to the intramuscular administration of quinine especially in debilitated and wounded patients. When adequate doses of quinine by mouth failed to act it usually transpired that the drug had not been taken in the doses prescribed. The U.S.A. Army had recently adopted a standard treatment consisting of five

doses of 0.2 gm. of mepacrine on the first day and three doses of 0.1 gm. on each of the following six days. With each of the doses on the first day 10 grains of bicarbonate of soda were given. Suppressive treatment should be started a fortnight before entry into a malarious area when this was impossible a dose of 0.2 gm. of mepacrine should be given daily for 4-5 days to begin with. While pamaquin [plasmoquine] greatly reduced the relapse rate in chronic benign tertian its effect on relapses occurring within the first four months was not so pronounced so that in certain areas its use was left to the discretion of the medical officers.

Several of the specialists at the meeting expressed concern at the large number of cases of blackwater fever that occurred after the standard courses of pamaquin all of these cases had been in Indian or Burmese patients and it was suggested that the doses were too large for light weight persons. Some speakers referred to the large percentage of relapses that occurred after the standard army treatment and examples were given of evasion by patients. In one instance it was found that 50 per cent. of the patients admitted for malaria while they were supposed to be taking suppressive treatment had no mepacrine in their urine. Similar evidence of evasion was found in 20 per cent. of a group of 1 000 men.

It was stated that a study of the case sheets of patients who had died of malaria showed that the diagnosis and treatment were often delayed one or two days longer than was necessary.

The Dengue Group—An Indian speaker proposed the adoption of the name dengue group of fevers and the inclusion of sandfly fever in this group under the name phlebotomus dengue. His views on the subject of the fevers of the dengue group were strikingly similar to those long held by the reviewer and apparently they were formed independently.

Kala azar—One specialist dealt with the diagnosis of the disease in Europeans in India. He had seen 10 cases in 1943 among British Other Ranks. The aldehyde test was negative in all the cases. The features common to every case were pyrexia without toxæmia enlargement of the spleen and progressive leucopenia. Leishman Donovan bodies were found by sternal puncture in eight of the cases but in the other two spleen puncture was needed and even then it was only after prolonged search by an expert that a single parasite was found.

Sprie—Reference was made to what appears to have been an explosive outbreak in which more than 100 cases were said to have occurred among British soldiers in the Chittagong area during 1943 all recovered when placed on a suitable diet. No clinical description is given of these attacks and it seems doubtful whether they were cases of classical sprie.

Other subjects discussed were neurology psychiatry tuberculosis the typhoid fever radiology drugs, medical training and the recently established Review Medical Board.

Lieut.-General Gordon WILSON Director of Medical Services in his opening address said that one of the chief objects of the Conference was to promote the drive to secure better clinical standards in the hospitals. To have done so much within three days to achieve this object is certainly a feat which reflects great credit on him and all concerned in organizing the Conference.

John W. D. Megaw

MANSON BARR, P. E. C. & GUYER O. K. G. *The Diagnosis and Management of Pyrexia in Wartime (with special reference to Africa)* J. Roy Army Med Corps 1944 Oct v 83 No 4 172-6.

Although this paper has been written with special reference to Africa most of its contents apply to fevers of the tropical and subtropical world in general. By judicious selection and economy in words the authors have managed to deal in four pages with a surprising number of problems of diagnosis and treatment.

Malaria is rightly given first place among the diseases that are discussed. A sharp distinction is made between the malaria of life-long residents in areas of high endemicity and the malaria of recent arrivals in infected localities. The disease is seldom a serious problem among those who have become immune by repeated attacks—in them the finding of parasites does not necessarily mean that they are suffering from malaria as their chief disease and it is only when their resistance has been broken down by some intercurrent illness that the infection is likely to demand urgent measures. In non-immunes malaria is an emergency which calls for immediate diagnosis and prompt treatment. The disease may be of serious importance even in cases in which parasites cannot be found, and the correct procedure is to give quinine at once unless malaria can be excluded. The Tanret test should be carried out to find whether the drug is being absorbed—if quinine is not being excreted by the urine an intramuscular injection is advised. [Many malarialogists believed that a negative Tanret test usually means that the drug has not been taken in the prescribed doses.]

Examples are given of the help that can be obtained from repeated counts total and differential, of the leucocytes.

In connexion with amoebic fever the authors state that the only practical method of diagnosis is the discovery of *E. histolytica* cysts in the faeces and added to this may be response to emetine. [Here again it might have been well to point out that the finding of cysts in patients who have lived for a long time in an area where amoebic infection is common is on a par with the finding of malaria parasites in comparable conditions. So large a percentage of the inhabitants harbour cysts that the presence of these loses much of its significance. If however the emetine test is carried out as is suggested by the authors there will be few failures in the management of this important disease.]

The numerous practical hints contained in the paper will be very helpful to medical officers who have limited experience of tropical fevers.]

John W. D. Meqar

TRU R. Pseudo-Tuberculosis of the Lungs with Eosinophilia, or Benign Eosinophil Leukaemia. *Indian Med Gaz* 1944 Nov v 79 No 11 511-14 4 figs on pl No 23

The author has seen and studied several cases of this interesting pulmonary condition associated with high eosinophilia and gives details of some of them in the present paper. With exception of the eosinophilia the symptoms are very variable—there may be no fever or it may be high, to 104°F., especially after injections of the curative arsenic—lung symptoms may be altogether wanting or may be severe without radiological signs—on the contrary there may be gross radiological changes even with absence of lung symptoms—the onset may be sudden with symptoms of acute asthmatic attacks or there may be a history of bronchitis for several months.

Details of six cases are given, each illustrating one or more of these points and so stressing the differences between them. All showed a high eosinophilia in one it was up to 80 per cent in a total count of 28 000. One the last to be related, is of special interest because pulmonary tuberculosis was present also.

The author discusses the suggested aetiology—in particular allergy and the existence of lung-worms. He quotes as favouring the allergy theory FRIMODT MÖLLER and BARTON (see this *Bulletin* 1941 v 38 539) and WEINGARTEN (*ibid.*, 1943 v 40 407) [But the writer of the former article stated—much in the clinical entity points to allergic origin chiefly because the eosinophilia dominates the syndrome described. But it is possible that there may not be a single agent which causes such a condition, but several." In the words of

WEINGARTEN At first an allergic state was thought the most likely explanation but as more cases were examined, this interpretation could not be accepted.] Lung mites as found by CARTER WEDD and D ABRERA [this *Bulletin* 1945 v 42 73] may account for some cases with respiratory symptoms but not for such as have no signs clinically or radiologically.

The author states that it is obviously an infectious disease accompanied by fever swelling of the lymph-glands and eosinophilia [but he brings forward no definite evidence in proof of this and the statement is purely a *petitio principis*. Lastly is it wise to use the term Pseudo-Tuberculosis for a condition in which there may be no fever at any time in which lung symptoms may be absent and when actual tuberculosis of the lung may co-exist?]

H Harold Scott

VISWANATHAN R. & NATARAJAN B Cold Agglutination in Tropical Eosinophilia. *Lancet*. 1945 Feb 3 148.

Sixty-six cases of tropical eosinophilia have been observed the sera of 61 were tested for their titre of cold agglutinins and five cases of atypical pneumonia and 39 cases of other conditions were also tested. Titres from one in 16 to one in 2 048 were observed in 87 per cent. of the tropical eosinophilia cases 90 per cent. of the atypical pneumonia cases and 33 per cent. of the cases of other diseases. Strong positive titres (greater than one in 256) were seen in 44 per cent. of the tropical eosinophilia cases and in three of the five atypical pneumonia sera.

[A misprint in the table makes it appear that 77 per cent. of the other diseases had a similarly high cold agglutinin titre. The figure should be 7 per cent.]

Titration were read with the naked eye. Dilution tubes had been allowed to stand overnight at a temperature of approximately 8°C. John F Loutit

MILLER, H. Transitory Lung Infiltrations accompanied by Eosinophilia. Report of a Case. *New England J of Med.* 1945 Jan. 4 v 232, No 1 7-10 3 figs. [23 refs.]

SCHRAMM M. A Fever Epidemic with Eosinophilia. *Acta Med Orientalis* (Palestine & Near East Med J) 1944 Sept.-Oct. v 3 No 5 148-8

The usual history of those attacked in this outbreak of thirty cases [the population is not given] is that after a prodromal period of 12-24 hours the onset is sudden with chill or actual rigor malaise a temperature 38.5-40 C. for 3-6 days with severe general pains nausea perhaps vomiting severe abdominal pain facial swelling and blotchy rash of limbs and trunk quickened pulse enlargement of spleen in some. All showed marked eosinophilia from 18 to 55 per cent. with total leucocyte count up to 12 000. Temperature fell by pseudo-crisis [presumably rapid lysis] on the third to sixth day but the debility might be considerable and convalescence slow eosinophilia to 20 or even 25 per cent. persisted for a month or more. Several of a family might be attacked, but not all simultaneously.

The author in discussing the diagnosis considers trichiniasis dengue sandfly fever and tropical eosinophilia. Dengue and sandfly fever are excluded because of the leucocytosis and eosinophilia tropical eosinophilia by the course of the disease and the absence of lung signs. Infestation by *Trichinella* he rules out because all in a family did not fall ill at the same time and the eating of pork was denied though all the patients were Christian Arabs who do eat pork. [The disease might be one of the dengue group (no mention is made of the existence or prevalence of *Aedes*) but the history and symptoms point strongly

to trichiniasis. Judging by investigations which the reviewer has made from time to time into food poisoning outbreaks we can rely little on the denial of eating pork again, in outbreaks of trichiniasis the fact that *all* in a family are not attacked at the same time has no weight all parts of the meat might not be equally infested, all might not eat the same amount at the same meal. To refrain from taking specimens for biopsy as the author did, because all members of a family did not show symptoms simultaneously was to deprive himself of the surest means of diagnosing trichiniasis or of the chance of excluding it.]

H Harold Scott

GENERAL PROTOZOOLOGY AND PROTOZOAL DISEASES.

- i. ADLER, S & PULVERTART R. J. V. The Use of Penicillin for obtaining Bacteria-free Cultures of *Trichomonas vaginalis* Douglé, 1837. *Ann. Trop. Med. & Parasit.* 1944 Dec. 30 v. 38 Nos. 3 & 4 183-9
- ii. MAHMOUD A. H. Isolation of *Trichomonas foetus* (Ridmiller 1923) in Bacteria-free Culture by the Use of Penicillin. *Ibid.* 219-22. [13 refs.]

These two papers deal with methods of obtaining cultures of trichomonas free from bacterial contamination.

i. Bacteria free cultures of *Trichomonas vaginalis* were first obtained by TRUSKILL and PLASS (*Amer. J. Obst. & Gynaecol.* 1940 v. 40 853) in 1940 but this was entirely accidental and was due to the fact that the bacteria in a mixed culture died out leaving the trichomonas alone. The reasons for the death of the bacteria were not determined so that it was not possible to repeat the process. It occurred to the authors of the present paper that penicillin might clear a culture of bacteria. The flagellate was inoculated directly into the following medium—Locke's solution 4 cc. inactivated goat serum 0.5 cc., septamide " (Heyden) [a Mg derivative of chloramine] (17 per cent solution) 0.1 cc. and rice starch. Growth was profuse and subculture was made on to the same medium to which sufficient penicillin had been added to give a concentration of 60 units per cc. The trichomonas grew well and was freed from bacteria. Subculture was made into medium containing 230 units of penicillin per cc.

ii. In this paper the author reports that penicillin was successfully used to obtain bacteria-free cultures of *Trichomonas foetus*. The medium employed consisted of inactivated horse serum covered with Douglas meat digest broth to which had been added 24 per cent glucose, the pH being lowered to 6.8. To this medium before inoculation with material containing the trichomonas, penicillin was added to give a strength of 30 units per cc. The medium was covered with liquid paraffin. The trichomonas grew well and were found to be free from bacteria. Subcultures in the same medium without bacteria were carried on successfully.

C M Heyden

GENERAL ENTOMOLOGY

- WATSON M. Elevage du *Taeniohynchus* (Coquillettia) *metallicus* Theobald [Rearing *T. metallicus*] *East African Med. J.* 1944 Sept., v. 21 No. 9 269-72, 1 pl. facing p. 273.

It will be remembered that the larvae and pupae of *Mansonoides* and related genera are attached to roots and stems of water plants beneath the surface

they possess piercing organs which penetrate the internal atmosphere in the plant and the larvae and pupae derive their oxygen from that source. In general these insects are difficult to rear in captivity for the broken pieces of plant tend to decompose and the larvae (though they can swim about) cannot for long use atmospheric air at the surface.

The author rears these larvae in a most ingenious way. He uses a particular type of very cellular packing paper full of air spaces and immerses strips of this in the water. Larvae pierce the paper and make use of its internal atmosphere. By this method several species have been successfully reared from egg to adult in the neighbourhood of Stanley Pool, Belgian Congo.

The author describes and figures a number of anatomical points. The subgenus *Coquillettidia* is consistently spelt *Coquillectidia* which appears to be a pure lapsus calami. P. A. Buxton

WAMAMAKER, J. F. An Improved Method for Mounting Mosquito Larvae. *Amer. J. Trop. Med.* 1944 Nov. v. 24 No. 6 385-6

FELDMAN MUHSAM, B. A Note on the Conditions of Pupation of *Musca domestica vicina* (Diptera) in Palestine and its Application. *Proc. Roy. Entom. Soc. of London Ser. A. Gen. Entom.* 1944 Dec. 29 v. 19 Pts. 10-12 139-40

The author points out that in Palestine it is not generally true that full-fed larvae of *Musca domestica* emigrate from damp manure to find a dry environment in which to pupate. Either because of climatic conditions or because of biological differences (the prevalent house fly is *M. domestica vicina*) fresh manure dries and forms a crust quickly and both larvae and pupae are found beneath this crust at about four inches from the surface. [It seems that the author refers here to cow dung rather than horse manure.]

If cow dung is kept in jars and moistened full-fed larvae emigrate at night and can be collected in a suitable dish or tray. One may collect larvae for poultry food using a series of large clay pots filled with dung on successive days and moistening them when the larvae are nearly full grown. Larvae contain 18.6 per cent. protein, 5 per cent. fat and 5 per cent. other solids (on a wet weight basis); they are rich in riboflavin (3 mgm. per 100 gm.) poor in carotins, and without vitamin A.

In field control one may use a trap on the Baber principle, heaping the manure on a platform surrounded by a gutter but it is essential to moisten it to cause emigration. P. A. Buxton.

MACGREGOR, I. M. A Case of Accidental Intestinal Myiasis. [Memoranda.] *Brit. Med. J.* 1945 Jan. 6 14

A normal healthy man of 22, having breakfasted heartily at 7 a.m. collapsed one and a half hours later with cold sweat and desire to defaecate followed by nausea, vomiting and vertigo. At no time was there abdominal pain. Admitted to sick quarters he was put to bed, kept warm and given only fluids. Retching was controlled by a few drops of tincture of iodine. A stool passed in the afternoon was loose and full of blood and mucus; no pathogens were isolated in the laboratory. An ounce of castor oil was given and no solid food allowed. He had a temperature of 101 F and severe headache but the symptoms passed off by next day. He had a strong desire to eat which is unusual in cases of acute bacillary dysentery. A stool passed that day contained numerous live and active larvae of *Stomoxys calcitrans* which in the absence of other pathogens were assumed to be causative. More castor oil was given and the patient recovered completely by the sixth day when normal diet was restored. No more larvae

were found after the third day. The larvae probably developed from eggs laid on some fruit which had been eaten without washing or examination.

J. R. Buxine.

MARTIN R. Sur la pathogénie de la paralysie ascendante à tiques. [The Pathogenesis of Ascending Paralysis caused by Ticks.] *Arch. Inst. Pasteur d'Algérie* 1944 June v 22, No. 2, 125-30

The author presents a new theory to account for the erratic appearance of tick paralysis. He suggests that this phenomenon is rare and irregular because it depends on the development of a certain rare syndrome in the man or other mammalian host. It will be recalled that other theories about tick paralysis have sought to explain it in terms of a problematical virus or of some irregular factor causing the ticks themselves to be toxic under unusual conditions.

In reviewing the main facts the author reminds us that paralysis may follow the bite of a large number of species of Ixodid ticks and that it has a wide geographical distribution. It has, moreover, been observed in many sorts of mammals, most commonly when they are young. It is commoner if the tick is fixed to the head, neck or region of the spine—an important characteristic is the immediate relief of symptoms if the tick is found and removed. He points out that it is very difficult to reconcile these facts with either of the old views of causation. There is indeed no positive evidence to support the idea that there might be a virus or that there might be some quite unexplained change in the nature of the tick or its saliva. The fact that extracts of ticks or of their eggs are poisonous throws no light on tick paralysis which is so rare and erratic, even in places where ticks are exceedingly common.

The author goes on to state that medical men have recognized a type of paroxysmal crisis which is due to disturbance of the sympathetic nervous system—the commonest symptoms of this are vasomotor disturbances with or without convulsions. He puts forward the view that the ascending paralysis due to Ixodid ticks might be placed in the same category and points out with truth that in general convulsions are much commoner in young animals, e.g. children, than in adults and that they can be brought on by a number of apparently minor causes. He relates this to the fact that tick paralysis is much commoner in children than in grown-up people.

[The suggestion put forward is certainly interesting, and it must be admitted that the phenomenon is, at present, frankly mysterious and quite unexplained.]

P. A. Barton

LABORATORY PROCEDURES.

LILLIE R. D. Factors influencing the Romanovsky Staining of Blood Films and the Role of Methylene Violet. *J. Lab. & Clin. Med.* 1944 Nov v 29 No. 11 1181-87 1 fig. [20 refs.]

An investigation of various brands of Wright's stain has shown that irregularities of staining are due to the methylene violet content which is present in varying amounts. Furthermore, it has been found that stock solutions of eosinates of methylene blue and the azures in methanol, methanol and glycerol, and other solvents undergo progressive alteration to form the lower azures and methylene violet. The quantity of methylene violet compatible with good staining varies as to whether staining is carried out on a slide exposed to air or in a covered vessel. The presence of an amount of over 4 per cent. is tolerated in

the staining of an exposed slide only if the initial methanol content of the final staining mixture after the addition of distilled water is over 20 per cent. If the concentration of methanol is 30 or 40 per cent, the presence of 15 to 30 per cent. methylene violet distinctly improves the staining. It comes about therefore that for all concentrations of methylene violet which may occur an initial methanol content of 25 to 33 per cent. is necessary if good results are to be obtained in exposed slide staining. As alkali polychroming methods are difficult to control acid chromatic polychroming is recommended. For this 200 mgm. $K_2Cr_2O_7$ (or its Na equivalent) are used with one gramme of 86 per cent. medicinal methylene blue (or 160 mgm. $K_2Cr_2O_7$ if the zinc salt of methylene blue is used). This yields chiefly azure B. Its eosinate is relatively more stable in methanol than eosinates containing higher proportions of azure A such as result from the alkali method. A one per cent. glycerol methanol solution forms a stable stock solution for dilution as required with plain methanol to 150 or 200 mgm. per 100 cc. for the usual Wright staining technique. The paper is a highly technical one which must be consulted in full by those interested in the chemistry of Romanovsky stains.

C M Wemyss

HELANDER, S. Detection of Chemotherapeutics in Thin Sections of Tissue by the Aid of Fluorescence Microscopy [Correspondence] *Nature* 1945 Jan 27 109

Fluorescence microscopy has not been much used for the demonstration of the presence and distribution of drugs in tissues because the tissues themselves are fluorescent and the method of preparing the sections might produce changes in the distribution and concentration of the drug. The author froze the tissue in liquid air, dried it over phosphorus pentoxide *in vacuo* at $-40^\circ C$, then embedded it in paraffin, cut sections and mounted them on slides ready for microscopical examination.

Drugs whose fluorescence is not blue can be shown directly in the section e.g. Prontosil rubrum and Prontosil soluble have a strong red fluorescence which is visible even in a concentration of 1×10^{-10} gamma per cubic micron. Drugs with a blue fluorescence change colour in many cases after heating in an oven e.g. sulphathiazole turns yellow at $170^\circ C$ for 5 minutes the tissue remaining blue. Other drugs which can be shown by heating are sulphanilamide, sulphapyridine, papaverine, insulin and penicillin. Sodium salicylate on the other hand, retains its colour after exposure to $200^\circ C$ for five minutes while the tissue turns yellow. No special staining is necessary for the identification of the tissues.

J F Corson

YOUNG E. G. & RICE F. A. H. Leucocytosis as an Index of Pyrogenicity in Fluids for Intravenous Use *J Lab & Clin Med* 1944 July v 29 No 7 735-41 1 fig. [14 refs.]

A simple test for the presence of pyrogenic substances in fluids used for intravenous medication is very desirable and the authors, having taken note of the fact that the alleged leucocytic response to allantoin in man was proved to be due to pyrogen, have devised a means by which the content of pyrogen in a fluid can be estimated by noting the symptoms, temperature and white cell counts of dogs after injection. The stock pyrogenic solution used as a standard was made from a filtered suspension of *Pseudomonas aeruginosa* which contained 5-6 mgm. of nitrogen per 100 cc. The fluids to be tested were compared with dilutions of this in their effects upon dogs. 1-20 cc. were injected intravenously.

Leucocytosis was found to be the most sensitive index but the authors point out that the leucocyte count of dogs varies very greatly. It is necessary

therefore, to make counts before and after injection. The level of the leucocytosis produced is approximately proportional to the amount of pyrogen in the more dilute preparations. The lymphocytes do not show a response comparable with that of the neutrophils. Leucocytosis appears to have been maximal 3-12 hours after injection.

By this means "it is possible to detect the presence of pyrogenic substances at or below the level of concentration which will produce symptoms in man." An increase of 50 per cent. above the original leucocyte count is significant at 6 hours after injection.

Charles Wilcocks

REPORTS SURVEYS AND MISCELLANEOUS PAPERS.

HOOBESS D. W. The Central Medical School, Suva (Annual Report for 1943)
Fiji Legislative Council Council Paper No 17 1944 10-13.

During 1943 there were 48 students in residence and also six post-graduate students of the former 18 were in their first year 18 in their third, and 14 in their fourth year. There were no second year students because as a result of the change (in 1931) from a 3-year to a 4-year course no students were admitted in 1934 1938 and 1942. Ten administrations, from Fiji to Samoa, are now sending students. The teaching staff comprises one full-time officer and 12-15 honorary teachers.

The Central Medical School has now completed its first 15 years of service during which it has trained 190 native Medical Practitioners but 125 others had previously been trained by its predecessor the Fiji Medical School, in the period 1888 to 1923.

Charles Wilcocks

DREARD J. H. Health Education to the Rural Native School. *South African Med J* 1944 Dec. 23 v 18 No 24 417-18.

This article by a specialist in education, discusses certain defects in health education which, while familiar to all, are too often disregarded. They are the presentation of health teaching in the form of uninteresting rules the failure of the teacher to impart a knowledge of health in place of the usual mechanical recitation of unapplied facts the inability of many teachers to realize that in health education the learner provides in his own person the subject matter. A common failing in many schools is the division into water tight compartments of subjects all having a direct bearing on health, both individual and communal, such as physical training, domestic science and biology as well as physiology and hygiene.

In the rural Native school the key to the situation is the Native teacher all students-teachers take at least, a two years course in hygiene. Teacher training centres are established at missionary institutions nearly all of which are in Native Reserves. The health and sanitary facilities vary from centre to centre. After training, the teacher is then expected to perform miracles in his school under the depressing conditions only too well known to health officers abroad. By co-operation between the various authorities some progress has been made.

Despite the strong recommendation of the Interdepartmental Committee on Native Education (1935) that Medical Inspectors and trained nurses be appointed for pupils in Native schools nothing has been done to implement it. On the question of school feeding, a pertinent point is raised concerning the "2d. per meal per child" as to what should be recommended as the ideal

meal, one which is to protect as well as to fill. Sex education including instruction about the venereal diseases is lacking. The article concludes by advocating sound practical steps for co-operation and co-ordinating committees.

E Cochran

McGREGOR, M. Health Education for Rural Bantu Children. *South African Med J* 1944 Dec. 23 v 18 No 24 418-19

The major problems in the schools are poor nutrition and dirt. Amongst school children the author's findings were that in every age group the average height and weight records were distinctly less than the accepted average for Europeans. The view that this is due to an admixture with Bushmen and Hottentots is no longer held. It is evident that nutrition plays a part and an experiment has been planned to supplement the diet of rural school children with fats and fat soluble vitamins.

A point concerning School Feeding Schemes often overlooked by the non-medical administrator is particularly well brought out. It is that those who plan school meals in Native schools will miss a great opportunity if they fail to impress upon the children the facts concerning nutrition in such a way that the latter will apply them to home feeding. Correct teaching now will ensure better nutrition of the next generation. The scheme of feeding should be planned to develop in the child a taste for protective foods that will last for life.

The contrast between the standard of cleanliness in school and the actual conditions prevailing in the home make it imperative to train the children to acquire an active dislike of dirt. This is no easy task since water-supplies are inadequate. There is no relationship between the theoretical teaching concerning bowel diseases and helminthic infestations and its practical application for few schools possess even the simplest latrine. It is the usual disheartening story of financial and administrative difficulties. The major consideration the author states is the provision of health facilities at schools or children's clinics.

E Cochran

MACKIE, Janet W. Adaptation of Public Health Practice to Foreign Cultures. *Amer J Trop Med* 1944 Nov v 24 No 6 331-9

The author writes from the Medical Section Health and Sanitation Division of the Office of the Co-ordinator of Inter American Affairs Washington and very evidently calls upon a good deal of first hand knowledge in her discussion of a problem which though largely relating to the South American countries has the same importance for most backward places. She shows that it is not enough merely to know the medical problems of a country but that unless the sociological background and the cultural state of the people are taken into account there can be little hope of rapid improvement in the general health. In backward countries the important diseases are profoundly affected by the customs and thoughts of the people and between backward peoples and the nations which have full educational systems there are differences in the interpretation and evaluation of life which are so fundamental as to create barriers to mutual understanding great enough to interfere seriously with public health and other projects. In these communities moreover there is a lack of trained persons who can supervise whatever health measures are proposed, and who can explain and demonstrate them successfully.

The medical problems of South and Central America (and *mutatis mutandis* of most tropical countries) are tuberculosis high infant mortality typhus malaria pneumonia smallpox venereal disease malnutrition and hookworm

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DUGARD J. H. Health Education in the Rural Native School. *Mel J* 1944 Dec. 23 v 18 No 24 417-18.

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In the rural Native school the key to the situation is all students-teachers take at least, a two years course. Training centres are established at missionary institutes in Native Reserves. The health and sanitary facilities are centres. After training, the teacher is then expected to return to school under the depressing conditions only too well known abroad. By co-operation between the various authorities much can be made.

Despite the strong recommendation of the Inter-Commission on Native Education (1935) that Medical Inspectors be appointed for pupils in Native schools nothing has been done. On the question of school feeding, a pertinent point is 2d. per meal per child as to what should be the

Africans is necessarily lower than our own. Native races argue well from their premises it is these and not the logical processes which are at fault. A comprehension of elementary bacteriology is probably not beyond a properly taught child. The author might perhaps have added a note on the good effect that may follow the creation of good taste in such matters as cleanliness housekeeping and personal habits. Illiterate races are great imitators and readily follow examples set by others a fact which may be turned to good advantage just as it may produce ill effects if the examples offered are poor.]

Charles Wilcocks

FLOOD C. A. & SHERMAN W. Medical Care in the Belgian Congo. *Amer J Trop Med* 1944 July v 24 No 4 267-71

This is a brief description of medical organization in the Belgian Congo where great advances have been made in the last 50 years to improve the health of the 10 million inhabitants. More emphasis has been placed upon preventive medicine than on the care of the sick person and in 1940 there were 183 public health officers [garde sanitaires] working under the physicians in addition to 201 physicians. Most of the large industrial companies employ medical men (there were 81 such in 1940) and there are many medical missionaries. Medical education of the natives comprises a three-year course followed by two years of hospital work and then by an examination for the medical assistants courses for nurses are held.

The author gives an outline of the position with regard to the main diseases—malaria yellow fever trypanosomiasis [largely dealt with by the Forcarni organization] yaws venereal diseases leprosy [68 000 cases under treatment in 1940] tuberculosis and smallpox. The steps taken to control these do not differ greatly from those adopted elsewhere.

The impression conveyed by the author is of an efficient progressive organization coping with an enormous problem.

Charles Wilcocks

BAER L. S. & ALLEN R. R. Health Status of the Marshallese. A Preliminary Report. *Amer J Trop Med* 1944 Nov v 24 No 6 345-7

The authors have examined one fourth of the total population 1 100 out of 4,500 of the islands and atolls visited. To obtain an accurate idea of the prevalence of disease more will have to be done but the figures given are suggestive.

Approximately 15 per cent of children are stillborn and 25 per cent. of those born alive die before reaching the age of two years. Maternal mortality is high 10 per cent. The first and last of these are due largely to the fact that there is no prenatal care and mothers are attended by any woman who happens to be near when parturition begins. On only one island did the native medical practitioner take any interest in obstetrics.

As regards general sanitation (so-called) Water-supply is rain in cisterns or from brackish ground wells food is scattered on the ground and flies are everywhere faeces are deposited ubiquitously. The commonest diseases are Yaws—75 per cent of the children under 10 years present active yaws and is commonly called sypilis which has given rise to the idea that syphilis is prevalent, which is far from being the case. The authors saw no syphilitic chancres or neuro-syphilis and the gummatous skin lesions were more probably the result of yaws than of syphilis. They saw two cases of lymphogranuloma inguinale with the ano-rectal syndrome. A Frei antigen survey is planned for the near future. Tuberculosis is not common they found one case of tuberculosis.

[May 1945]

Infestation to deal with such a wide variety of conditions a balanced organization of which the local full-time Health Officer is the mainstay is essential. But the Health Officer must have his subordinate staff, and since the members of this staff are those who will come into the closest contact with the community it is essential that they should be fully aware of the habits of thought of the people. They should, of course, be recruited from the people among whom they will work, but should be so persuaded and trained in the logic of modern medicine that they can gradually break down the beliefs and fetishes which so often obstruct progress. The author makes the very valid point that provision of curative services should be ample, so that the confidence of the people may be obtained and opportunity taken to give elementary health instruction.

The epidemiology of a disease may be modified by the sociological pattern of a community. For instance, in one place in Bolivia, men and boys spend the nights guarding their crops from theft, and sleep therefore, near streams; the women and girls remain in the hills. The incidence of malaria in men and boys is markedly higher than in women and girls. Empirical knowledge of illiterate people concerning the epidemiology of one disease may determine the incidence of another—anopheles in a certain valley could be controlled, but because the people know the far greater danger (from Oroya fever) they would run if they lived and slept higher up the valley anopheline infestation from the uncontrolled higher parts is continuous. Knowledge of facts of this kind is essential to health control.

The author takes note of the fact that native medical art makes a strong appeal to the emotions, and that the detached attitude which serves very well in educated communities may repel the backward peoples. Yet she very rightly insists that it is through logic that modern health information should be introduced. Unexplained rules and regulations are seldom effective, but advice based on explanation accompanied by ample demonstration has a great future. An elementary appreciation of the bacterial origin of disease can be made if the people are shown living creatures in series of diminishing size, by means of lens and microscope (beginning the reviewer suggests, with such well-known parasites as the intestinal worms). Simple cultures of bacteria can be made and demonstrated. The people must be taught to protect themselves but they cannot adequately assimilate their lessons if they are given merely theoretical lectures. Instruction should begin in the schools, for it is the young who can most easily grasp the subjects.

The solution of the problem of approach lies in a change of emphasis in public health education at professional and postgraduate levels. Curricula must provide instruction for members of the health staffs of all grades, and the author is quite definitely in favour of a plan whereby although curative services of the highest quality are maintained at key centres special emphasis is placed on the deliberate training of large numbers of health workers destined to serve the rural areas. (The other programme suggested by some authorities that high professional standards cultivated in urban areas will gradually diffuse into the rural areas, will not she thinks, give such good results.) The rural workers of the villages would carry out such duties as vaccination, registration of births and deaths and certain sanitary duties they would give simple treatments and would be trained to instruct the villagers, by demonstrations, in the rationale of disease prevention.

(Many of the duties to which the author refers are carried out, at all levels in the British Colonies where in the medical services the local inhabitants are trained to all grades from fully qualified medical men to dispensers, tribal dressers and sanitary inspectors. She is undoubtedly right in emphasizing the need for a logical basis of instruction to the general public. It is probably a mistake to imagine that the sense of logic possessed, for instance, by the

Africans is necessarily lower than our own. Native races argue well from their premises, it is these and not the logical processes which are at fault. A comprehension of elementary bacteriology is probably not beyond a properly taught child. The author might, perhaps have added a note on the good effect that may follow the creation of good taste in such matters as cleanliness housekeeping and personal habits. Illiterate races are great imitators, and readily follow examples set by others a fact which may be turned to good advantage just as it may produce ill effects if the examples offered are poor.]

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peritonitis and one of laryngitis but saw only one with signs among 120 adults subjected to fluoroscopy. *Dengue* is frequent. *Dysentery* both amoebic and bacillary common and the latter is one of the most frequent causes of death among children. *Leprosy* occurs, but the authors saw only five cases. *Helminthiasis* is not common [no figures are given], flea-borne *typhus* is endemic. *tsutsugamushi* disease was not seen, nor any *Trombicula*. *malaria* was not seen, nor any *Anopheles*. A few cases of neuritis probably *beriberi* were met with and one case of cheilitis. Many of the natives have spongy hyperplastic gums which bleed readily. *Scabies* and *fungous infections* of the skin are rife and are ascribed to the use of unmountable clothing urged on them by the missionaries and now owing to the war reduced to the innerest rags and very dirty and there is practically no soap available. H. Harold Scott.

WIKERLAD, F. A. S. Dental Survey in the Marshall Islands. *U.S. Nav Med Bull* 1944 Dec., v 43 No. 6, 1141-4

GAUD, Jean, SALM, G. & FASSI, P. Parasitisme intestinal chez les écoliers de Fes. [Intestinal Parasitism among Schoolchildren in Fes.] *Bull. Inst. Hyg Maroc* 1943 v 3 87-113 [Bibliography]

The authors examined the faeces of 518 persons in Fes, Morocco for evidence of intestinal parasites. 398 were school children of Mohammedan schools in Fes and this study is concerned mainly with them. Altogether about 80 per cent. of the children had some species of intestinal parasite.

Helminths.—Of the nine genera which have been recorded in Morocco the authors found only five—*Ascaris*, *Enterobius*, *Trichuris*, *Taenia* and *Hymenolepis*. Those not found were *Ancylostoma duodenale*, *Strongyloides stercoralis*, *Fasciola hepatica* and *Schistosoma haematobium*. *Ascaris lumbricoides* was found in 60-75 per cent. *Trichuris trichiura* in 40-50 per cent. *Enterobius vermicularis* in 5 per cent. *Taenia saginata* in 1 per cent and *Hymenolepis nana* in 2 per cent.

Amoebae.—The following were found. *E. coli* 36 per cent. *E. histolytica* 14 per cent. *E. hartmanni* in two subjects, *Paradidymus* (*Didymosis*) *batschlii* or *Endodidymus nana* [diagnosis doubtful] fairly frequently.

Flagellates.—*Giardia intestinalis* 8-10 per cent. *Trichomonas intestinalis* 13 per cent. *Chilomastix mesnili* about 5 per cent. *Enteromonas hominis* about 10 per cent. and *Embadomonas intestinalis* in one person. They found also *Spirochaeta cingrata* in subjects and *Balanidinium coli* in two.

As a rule, intestinal parasites were most frequent in children under 10 years of age and were more frequent in children than in adults. The association of two or more species of parasite in one person was not, according to the authors' mathematical calculations, simply a matter of chance. Some associations were more frequent, others less frequent, than would be expected from calculation. More parasites were found in people who showed no symptoms attributable to them than in those with symptoms and the authors give a warning that the finding of parasites is not necessarily a diagnosis in a case of illness.

J. F. Corson

KEAY, B. H. The Blood Pressure of the Cuna Indians. *Amer J Trop Med.* 1944 Nov v 24 No 6 341-3 1 fig

A most interesting study (though unfortunately of a limited number) of the blood-pressure of members of a healthy native race. The Cuna Indians are Panamanians who used to live on the coast of the South American mainland, but more than a century ago because of a high death-rate, they moved to islands

of the San Blas Archipelago along the Atlantic coast. They live largely on vegetables and fruits (plantains, bananas, yams, mangoes, oranges, pineapples) and sugar cane supplemented by fowl, deer and peccary [*Dicotyles* (*Tavassu*) of the Family Suidae (*Tayassuidae*)].

The author reports on the systolic and diastolic blood pressures of 407 Indians, 263 males and 144 females, out of a total population of some 15 000. In the males the average systolic pressure ranged between 109.7 mm. among the 16-25 years age-group and 103.3 mm. at 36-45 years, 108.1 at 66 years and over. Only 10 of those examined were of this age. In the 56-65 age-group the average was 105.5 mm. [It will be observed with interest that the author confirms what others have found, that the systolic pressure among natives tends rather to fall than to rise with advancing age]. The average for all the males at all ages was 105.4 mm.

Among the females the average was 105.0 mm. and among all those up to the age of 65 years it remained between 104.3 and 105.6 mm. A higher figure (113.7) is given for those over 66 years of age, but this is of no true significance as only three of that age or over were examined. The average diastolic pressure was the same, 69.3 mm. in both sexes.

H. Harold Scott

BOOK REVIEWS

STRONG, Richard P. [M.D. Sc.D. D.S.M. C.B. Professor of Tropical Medicine Emeritus, Harvard University, etc.] *Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases*. Seventh Edition in Two Volumes. Vol. I. pp. xvii + 1-871. Vol. II. pp. vi + 872-1747 + xi. With 368 figs. & 3 pls. (2 coloured). 1944. Philadelphia: The Blakiston Company. [\$21.00]. London: H. K. Lewis & Co. Ltd. [£5.5s.]

This 7th edition of a famous textbook is dated October 1944. It is largely a reprint of the 6th edition [see this *Bulletin* 1943 v. 40: 953] with which the pagination corresponds, except that new material has been inserted, sometimes by change to smaller type, sometimes by insertion of paragraphs, and sometimes by insertion of pages numbered (for instance) 904a, b, c and d. The work is therefore slightly bigger than its predecessor and maintains the same layout and material with additions which indeed are comprehensive and up to date. There has not been much actual rewriting, and by the method of inserting whole pages of new material the flow of the narrative has been made somewhat disjointed—the new material is not always in just the right place. But the matter is there, and no doubt the demand for this work has been great enough to call for reprinting, and the editor is surely right in adding the latest information in whatever manner is most quickly achieved. It remains one of the best books in the world on tropical diseases.

Some idea of the extent of new information now included may be gained from the mention of the diamidines in treatment of trypanosomiasis and kala-azar, penicillin in experimental relapsing fever, DDT as a louse insecticide (but the statement that it is effective against louse ova (p. 950a) is incorrect), a description of Bullis fever and an account of recent transmission experiments in kala-azar.

There are however certain points which may be criticized. On p. 38 *Anopheles darlingi* is noted as an Old World species, and although a short list of Old World species important in malaria is given, such vigorous transmitters as *A. minimus*, *A. punctulatus*, *A. superpictus* and *A. calidifacies* are not included, though they appear in a general table on p. 43. [In this table incidentally, there are six mistakes of spelling.]

The chapter on leprosy needs additions on the subject of tuberculoid leprosy and on lepromum but the long addendum on yellow fever brings that subject well up to date. The classification of the rickettsial diseases is not satisfactory trench fever might well have been placed next to louse typhus and Bulha fever along with the tick borne group rather than with tsutrugamushi, with which it has little affinity. In the account of tropical ulcer more emphasis should, perhaps have been laid on the underlying element of malnutrition. In the discussion of tsetse in relation to African trypanosomiasis the importance of the different habitats of the different flies is not sufficiently stressed.

But these criticisms are of relatively minor points and should not be regarded as seriously affecting the high standard of this admirable work. The writing is clear and the accounts of disease are such that they present the subjects as they are and as they appear to the practitioner in the field, complex and not yet clearly understood. The mistake of over-simplification has been avoided, and the medical man who buys these two volumes will be able to find much help in the numerous accounts of the findings of other workers. The bibliographies appended to the various sections will help him to study further the subjects which take his interest. The illustrations are excellent.

For those who have not seen the table of contents it is enough to say that all the usual tropical diseases are dealt with and that there are appendices on clinical diagnosis, laboratory procedures, effects of hot climates personal hygiene and disinfectants.

Charles Wilcocks

KUBES Vladimir [D.M.V., Director del Instituto de Investigaciones Veterinarias Caracas]. El *Trypanosoma vivax* Americano agente de la Tripanosomiasis Bovina en Venezuela, su Comparacion con el del Africa. [American *T. vivax* the Causative Agent of Bovine Trypanosomiasis in Venezuela Comparison with that in Africa.] 3a Conferencia Inter americana de Agricultura Caracas Vo I Caracas 1944 pp. xi+124 20 figs., 10 tables & charts. [83 refs.] [In Spanish English Summary pp. 111-117]

Trypanosoma vivax the cause of Souma in booted animals, represents a remarkable instance of a tsetse-borne African trypanosome spreading widely beyond the area of distribution of its natural vector to remote countries. Having been introduced with cattle imported from Africa it has established itself in bovines in Mauritius the West Indies (Guadeloupe and Martinique) Central America (Panama) and South America (Dutch and French Guianas, Venezuela and Colombia). The only other known example of tsetse-borne trypanosomiasis outside Continental Africa is the occurrence of *T. congolense* in Zanzibar.

The present work is the first monograph dealing exclusively with trypanosomiasis due to *T. vivax*. It represents the results of observations and experimental investigations which the author who is Director of the Institute for Veterinary Research has carried out in the course of ten years in Venezuela, where *T. vivax* affects bovines causing in them a disease known as *Socadera Huapira* or *Cacho Huaco*. From the introduction and the section on geographical distribution it is evident that this disease is more common in Venezuela than is realized outside that country and it is of considerable economic importance causing outbreaks, with a high mortality (30 per cent) among local cattle. The succeeding sections of this book deal with the different aspects of *vivax* trypanosomiasis in Venezuela, where the disease presents certain peculiarities distinguishing it from the African Souma. On account of this and because the monograph contains a number of important new data, it is proposed to deal with some of these points more fully than is usual in a review.

From the account of the aetiology of the disease it is seen that morphologically the South American strain of *T vivax* (sometimes described as *T vivax*) is identical with the African ones. Attempts to cultivate this trypanosome proved unsuccessful. There have been no special investigations on the transmission of *T vivax* in Venezuela but it would seem that various blood-sucking Diptera are capable of acting as mechanical vectors. The author describes numerous attempts to infect mammals with local strains. In addition to bovines which are the only animals harbouring this trypanosome under natural conditions it is experimentally infective to goats and sheep and to a lesser degree to equines whereas other animals (including rodents) are refractory. In the section devoted to the clinical course it is stated that the disease may occur in acute form when it gives rise to epizootics with a high mortality or the infection may be chronic or even symptomless. The course of the disease depends primarily on the state of nutrition of the herd, being severe in undernourished animals and mild in those that are well fed. This variation was also confirmed by experimental infections in which the course of the disease could be favourably modified by improving the diet of the affected bovines. The chief diagnostic methods in *vivax* trypanosomiasis are based on the finding of the parasites by blood examination lymph-gland puncture and inoculation of susceptible ruminants. The section on therapy is of especial interest. After reviewing in detail the methods of treatment of *vivax* trypanosomiasis employed in Africa the author describes his own results in the treatment of Venezuelan disease with arsenicals and antimonials. While the former were without any effect the latter proved to be fairly effective if applied repeatedly in the early phases of the infection. However the author made the important discovery that Bayer 7602 [see this *Bulletin* 1942 v 39 820 *ibid* 1943 v 40 22] which is now employed for the treatment of Chagas's disease has a highly specific effect on *T vivax* infections. A single intravenous injection of from 2.5 to 10 cc. of the drug into bovines weighing 100 kgm. results in a complete cure while a dose of 1 cc. protects from infection.

Some interesting original observations are recorded in the section dealing with immunity. While in African strains of *T vivax* immunity is of the type known as preimmunity in Venezuela it develops in two phases during the first six months the host becomes preimmunized but some months later it acquires full immunity being protected against reinfection for at least two years. Among the methods of immunization tried the author favours artificial infection of the bovines followed by incomplete treatment with trypanocidal drugs whereas Schilling's method was found to be of no practical value since the course of the disease in young animals proved to be similar to that in adults. For prophylactic purposes the author recommends the institution of sanitary cordons as well as the treatment of infected cattle with Bayer 7602. The book is well illustrated by figures photographs numerous tables and charts and there is an adequate list of references.

This monograph is an important contribution to our knowledge of trypanosomiasis in livestock and should be of especial value to veterinary practitioners in the New World.

C. A. Hoare

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WEINMAN David. Infectious Anemias due to Bartonella and related Red Cell Parasites. *Trans Amer Philosophical Society* Philadelphia. 1944 Apr New Ser Vol 33 Pt 3 243-350 1 map & 6 figs. on 1 pl. Philadelphia The American Philosophical Society 104 South Fifth Street

This admirable work will probably remain the standard for reference for all interested in *Bartonella* and its congeners for a long time certainly until further discoveries are made to clear up the few outstanding difficulties such as

questions whether the Oroya Fever type and the eruptive phases depend on degrees of host immunity—what is the nature of development of the parasite in *Phlebotomus*—the significance of asymptomatic human cases—to what class does the *Bartonella* group belong?

Dr. Weinman undertook to gather together all that is at present known of the organisms and the diseases they produce and to put forward the information in a summarized form and he has successfully accomplished his self-imposed task to the lasting benefit of the parasitologist, the bacteriologist, the protozoologist and the clinician.

Human bartonellosis and its animal analogues are important on several counts among them the fact that the human disease is acquiring a more extensive field of action than has been supposed, that many animals are infected without presenting symptoms—that a combined study of the human and animal form may throw much light on the aetiology, pathogenesis and treatment of blood diseases, while the fact that many animal infections are latent until splenectomy is performed has an important bearing on the immunological function of that viscus.

This monograph serves the two-fold purpose of putting before us in a connected story all that is at present known and pointing out what needs further investigation and thus stimulating research.

The whole work consists of two main parts in four chapters. The first and last chapters are concerned with human bartonellosis and its public health aspects, the second with animal bartonellosis and the third with the closely allied *Eperythrozoon*. One very important factor contributing to the value and success of an up-to-date summary of any condition is a full list of references with accurate details. This is not infrequently omitted from epitomes in other respects excellent, but is a special feature of the work under review. The documentation is most detailed, the name and year being given in the running text and the full reference in a very complete bibliography. To the first chapter on human bartonellosis there are over 300 references. The reviewer has not verified them all, but a large number of them are papers which have been abstracted in the *Tropical Diseases Bulletin* and those he has been able to verify and has not found any mistake in them.

The chapter on Human Bartonellosis deals with every aspect of the question, its history, geographical distribution, clinical types, pathology and experimental production, "asymptomatic disease, epidemiology and transmission, latent infection and immunology and treatment. The chief points in connection with these are within the knowledge of readers of this *Bulletin* or can easily be looked up—but to have them all brought together in a single work, such as this, is a great boon.

As stated above control and the public health aspects of human bartonellosis are discussed in the final chapter. The disease is existent not merely in a few endemic foci in South America but may assume epidemicity as in Peru in 1870 when 7 000 deaths are estimated to have occurred from it, and in the Colombian outbreak, where in a single department 4 000 are said to have died of it out of a population of 100,000. There is no reason to think that infection may not spread far wider and thus become a menace and a public health question of the highest importance. Since an insect vector (*Phlebotomus*) is responsible for practically all infections and since no effective therapy is known as yet for eradication of human infection, the only available measures of control must consist of those aiming at reducing the numbers of *Phlebotomus* and those directed to avoiding contact between patients and uninfected insects on the one hand, and infected insect and uninfected man on the other. Observation of the habits of *Phlebotomus* has shown that, in certain districts at least, it bites only at night, so workmen (for example, those engaged in building the Puente Carrón over the Rímac

River) are taken out of the district before nightfall or are transported to the higher levels for the Peruvian species of *Phlebotomus* are not found where the night temperature is below 55°F. *s.c.* at 8 000 feet or more. Where this is not feasible—and mass emigration would come within this category—*Phlebotomus* proof buildings should be erected windows and doors screened and walls roof and floors be smooth and solid to prevent breeding and access of the flies outside the filling in of crevices in rocks or masonry DDT should find a place.

It is to be noted that none of the three species of sandfly present in Peru *P. noguchii*, *P. peruensis* and *P. verrucarum* was caught in Columbia collections hence in the latter State either the species involved was different or some other vector than *Phlebotomus* was concerned. Care must be exercised also to guard against the introduction of an infective person into a *Phlebotomus* infected zone and of non immunes into endemic areas.

In Chapter II the Animal Bartonellooses are described and their significance and characters discussed. The position of *Haemobartonellae* in the Natural Order is not yet determined. They would seem to be most closely related to Bacteria but if so they are of an atypical and distinct group. They differ from *Bartonella*—the cause of human disease—in that they have not been shown to develop outside the blood and do not produce cutaneous eruptions moreover unless resistance or immunity is lowered by removal of the spleen they do not cause disease. They are of much wider perhaps world wide distribution, are transmissible by direct blood inoculation and are readily affected by arsenotherapy. The author deals in turn with *H. muris* (found all over Europe in North and South America in the Near and Far East and in India) which is often present as a latent infection of white rats and may infect mice rabbits and other rodents and if splenectomy is performed sets up a definite macrocytic type of anaemia. The account of the anaemia its characters and course the pathology and pathology of the disease produced the morphology cultivation and results of experimental inoculation of blood and liver suspension or of laked blood into rats white mice guinea pigs rabbits hamsters monkeys and pigeons splenectomized and non-splenectomized, are related to the transmission by the agency of lice *Polyplax (Haematopinus) spinulosus* and the existence of natural immunity or production of acquired immunity are discussed. Instances of natural immunity that is immunity in rats in spite of splenectomy have been shown to be due in many if not in most cases [perhaps in all] to the existence of supplementary spleens in these animals.

Haemobartonella canis of the dog is described and considered on the same lines as *H. muris*. It has been seen in Europe India Africa and North and South America. Also *H. bovis* of oxen *H. microti* of the vole *H. sturmanni* of the buffalo *H. tyzzeri* of the guinea pig and a few others of undetermined rank are dealt with more briefly. Twenty-one species are named as having been encountered in the literature.

In Chapter III the question of *Eperythrozoon* is debated—its place in the Natural Order and its affiliations. Descriptions of seven named species their appearances in the blood after splenectomy the results of experimental inoculation of blood of white mice containing the parasites *E. coccoides* into laboratory animals natural transmission by the louse *Polyplax serrata* are all considered at length and similarly as regards *E. ovis*. Others are treated more briefly but adequately regarding what is known of them. Animal haemobartonellooses and eperythrozoonoses have a bibliography of nearly 400 references. A well reproduced plate shows four figures of human bartonellosis two of the blood one of an Oroya Fever lymph node and one of a section of a verruga. In these the different types of parasite are seen the rods small chains.

dots and rings and in the Oroya lymph-node rounded clumps of these within the endothelial cells of a vein. Another figure shows the rods, coccoid and minute ring forms in a blood film of a splenectomized mouse infected with *Harmobartonella microti* and lastly one of *Eperythrozoon coccoides* from a white mouse.

In conclusion, the whole work has been well carried out and, as already stated, until more discoveries have been made it could not, in the opinion of the reviewer be bettered.

H Harold Scott.

GUASCH, Jorge. Paludismo Kala Azar Fiebre Recurrente. [Malaria, Kala Azar and Relapsing Fever] 475 pp. 24 figs. & 10 pls. (8 coloured) Monografías "Miguel Servet." 1943. Madrid Barcelona Editorial Miguel Servet. [27s. 8d.]

The work here reviewed deals in much but not too much detail with malaria, leishmaniasis and relapsing fever as affecting Spain. The first has so many features in common in whatever part of the world it prevails that this monograph will be found to be almost generally applicable. It occupies the first 300 pages, while to kala azar are given 102 and to relapsing fever 55 pages. As this work purports to treat of these diseases as they affect Spain only remarks on other countries are but occasional or incidental. Nevertheless, as regards Spain at least, this book brings our knowledge very much up to date (1943) and is a most valuable guide.

To pass on to more detail. Malaria is dealt with under the usual headings of geographical distribution in the world (shown in a Table giving the relative percentages of the different infecting plasmodia) and in Spain in particular (a map with varied shading shows the intensity of prevalence) the plasmodia and their life-histories, transmission clinical pictures prognosis, diagnosis treatment (with remarks on the different drugs used) prevention by treatment of patients and of carriers by antilarval and antoosquito measures and the organization of an antimalaria service (only a couple of pages are given up to this). Some interesting figures are given regarding the effects of malaria in interrupting pregnancy or in killing the foetus. It causes abortion in 8-16.5 per cent. of pregnant women with untreated malaria, in 19-47 per cent. it causes premature birth, and in as many as 32-65 per cent. results in a dead-born foetus. The chief danger is from subtertian malaria.

Among the usual antilarval prophylactic measures, petroleum, Paris green, Gambusia general sanitation, planting of trees bonification, etc. two others for local application, not widely known are mentioned, namely cactus paste and Stoxal. Both are French preparations. The former is used in Northern Africa cactus leaves are sliced, then macerated in water till a mass is formed which decomposes it is then spread over collections of water where it forms a coating which impedes the respiration of the larvae it is said to be effective for weeks even months. The latter Stoxal is solid triformol which is mixed with dust or fine ash in a proportion of 2-5 per cent. and spread like Paris green. It has the advantage of being harmless to vegetation, to fish and cattle, and is cheaper than Paris green.

A number of remedies for the treatment of blackwater fever are mentioned, including snake antivenene [see also SIXCH & SIXCH, this Bulletin 1944 v 41 927]. None of this is of much use as nothing is said as to details of administration and the doses even are omitted for many of them. The pathological anatomy of malaria is described in half-a-dozen pages.

Kala azar as it affects Spain, is equally clearly presented the pros and cons of the identity of human and canine leishmaniasis are put very fairly but this part contains nothing new or which is not mentioned in Wenyon's classical work. The clinical picture of the disease as it affects children and adults is

given separately and the diagnosis and treatment are adequately described remarks are made on diseases complicating leishmaniasis especially tuberculosis (the existence of which states the author is common but does not affect the prognosis) diphtheria (which is usually fatal) and whooping cough measles and scarlet fever which seem to bring about a rapid regression of the kala azar [Have other writers found this?] The pathological anatomy is given briefly in three pages.

Lastly relapsing fever not infrequently occurs together with malaria and the former may develop even while full treatment is being given for the latter. García de Cosa has reported several cases of this association some with *P. vivax* others with *P. falciparum*. A map shows the distribution of cases in the Lerida outbreak of 1938-39. A useful short table gives the chief distinguishing features of the Spanish tick borne and the ordinary louse-borne types of relapsing fever —

Spanish type

- 1 Commonest from May to October
2. Outbreaks small and limited in spread.
- 3 Usually 4 or 5 febrile periods rarely 3 or 6
- 4 Prognosis favourable
- 5 Cure often spontaneous salvarsan ineffective.

Louse-borne type

- 1 Mainly a winter disease February and March
2. Often widespread.
- 3 Usually 2 or 3 febrile periods occasionally only one. (Those with 4 or 5 are probably not louse borne)
- 4 Prognosis more grave
- 5 Neosalvarsan usually quite effective

There is no real index the index so-called is merely a detailed list of contents but this is so full that more is hardly needed. As with other books of this series a full or even extensive bibliography is not attempted but in the list of the most important works consulted it is gratifying to note that special mention is made of the *Tropical Diseases Bulletin* and of the *Transactions of the Royal Society of Tropical Medicine and Hygiene*.

In conclusion though in paper covers the book is strongly bound and well got up the illustrations are good and the coloured plates well reproduced charts and diagrams are clear. The proofs have evidently been very carefully corrected for we have found no misprints.

H Harold Scott

DAS GUPTA B M [Professor of Protozoology and Director Calcutta School of Tropical Medicine] Knowles's *Introduction to Medical Protozoology* 2nd Edition revised and abridged. pp xvii+323 With 104 illustrations & 10 coloured pls. 1944 Calcutta U N Dhur & Sons Ltd. 15 Bankim Chatterjee Street College Square [Rs 20/]

In 1928 Robert KNOWLES published in India his *Introduction to Medical Protozoology*. This work as the author whole-heartedly admitted was based very largely on the reviewer's *Protozoology* published in England two years before. Knowles's book was intended chiefly for the use of students in India and has been extensively used in that country. In 1936 Knowles died and the task of preparing a second edition has fallen upon his successor in the chair of Protozoology at the Calcutta School of Tropical Medicine Professor B M DAS GUPTA who was Knowles's assistant.

The second edition differs from the first in that it is shorter and cheaper as a result of removal of those sections which are only remotely connected with the subject of medical protozoology. What remains has been thoroughly

revised and brought up to date as regards knowledge acquired since 1928. The result is a book of 323 pages instead of the 887 of the first edition. From the point of view of the student of medical protozoology who needs only information regarding the parasitic protozoa of man the book offers all that he can want while sufficient references are made to the allied parasites of animals to indicate that there is a wider field into which he can enter by studying the larger and more comprehensive treatise. It is only natural that frequent references are made to conditions existing in India and in the author's own experience, and as the book is intended primarily for the Indian student this undoubtedly adds to its value. The book is particularly free from mistakes so that students whether in India or elsewhere can rely upon it as giving the latest information on the protozoa which are of medical importance. In some places it would have been possible to give more details but this would have increased the size of the book, which the author was at pains to avoid.

Apart from the protozoa, descriptions are given of a variety of organisms which students of protozoology are likely to encounter in their work. These come under the headings *Toxoplasma*, *Rickettsia*, *Chlamydozoa*, *Anaplasma*, *Grahamella*, *Rhinosporidium*, *Histoplasma*, *Cryptococcus*, *Blastocystis* and *Spirochaetes*. A final section deals with laboratory methods in a very complete and useful manner. It seems that some of the staining methods which appear in the section on malaria would more appropriately have been included here. However this is a small matter of little importance. The illustrations are excellent especially the 10 plates, which as regards detail and colour are distinctly superior to those of the first edition. It seems unnecessary to describe the book in greater detail suffice it to say that in the reviewer's opinion the book is a thoroughly good one which successfully achieves all that the author undertook to carry out. It can be recommended to all those who wish to study the parasitic protozoa of man and the various diseases and pathological conditions they produce.

C. M. Wexon

TROPICAL DISEASES BULLETIN

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[No 6

SUMMARY OF RECENT ABSTRACTS *

V LEISHMANIASIS

VISCERAL

Epidemiology Aetiology

In recording 136 cases of kala azar in the East African Forces ANDERSON (p 17) makes the point that the disease is much more common in northern Kenya and southern Abyssinia than was formerly supposed. Most of the infections occurred during the wet season April to June and the average incubation period was 13 weeks. [See also COLE below.] FERRO-LUZZI (p 194) records nine cases of kala azar in Eritrea. Though it has previously been reported in man and dogs in that area it is not common.

THOMPSON (p 273) reports a case of kala azar in a seaman who had served in Malta and was presumably infected there. LIPSCOMB and GIBSON (p 550) also report a case of kala azar in an adult presumably contracted in Malta. They note that in spite of the characteristic clinical picture it was many months before the correct diagnosis was made.

PEÑA YÁNEZ (p 192) having noted certain similarities between kala azar and subtertian malaria conceived it possible that there might be a cycle of development in *Leishmania donovani* comparable with that of *Plasmodium falciparum* and linked in a similar manner with the febrile exacerbations which are a notable feature of some cases of kala azar. By means of frequent examination of spleen or sternum puncture material he claims to have found evidence of such a cycle of development in the parasite. He describes the various forms seen and estimates that the cycle typically occupies 24 hours most of the parasites are extracellular and are in the process of multiplication when the attack of fever comes on. If the patient does not show the daily rise of temperature it is likely that there will be irregularity of the cycle.

NATTAN LARRIER *et al* (p 931) have found the N African jird (*Mersones shawi*) more suitable than the golden hamster (*Cricetus auratus*) for experimental work with Mediterranean *L. donovani* but less suitable than the spermophile (*Citellus citellus*)

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1944 v 41. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

Clinical Findings.

COLE (p. 831) gives a detailed description of 60 cases of kala azar in East African Native troops. The infections were contracted near Lake Rudolph or elsewhere near the Kenya Abyssinia border and the incubation period, which could be assessed fairly accurately was from two to four months. The clinical features included abdominal pain, diarrhoea, characteristically irregular fever but with a remarkable degree of physical fitness. Enlargement of spleen and liver occurred relatively late, and glandular enlargement was present in half the cases. A rash was seen in many cases—this began on the face and spread to the trunk and arms, and in some cases progressed to form warty growths. Leishmania were present in scrapings from these skin lesions, and it was noted that the rash, though common in patients who recovered, was found in only one of the 22 fatal cases. In diagnosis gland puncture should first be made, followed by spleen or marrow puncture if necessary and scrapings of skin lesions should always be examined. BURKE (p. 833) comments on the statement by Cole and his colleagues that abdominal pain is a feature of kala azar and remarks that in his experience in Assam, abdominal pain is almost a diagnostic symptom.

SHELLIM (p. 833) describes a case of kala azar in which the liver but not the spleen, was enlarged. This gave rise to a suspicion of hepatitis but leishmania were cultivated from blood and sternal marrow.

Though acute agranulocytosis has often been reported as a complication of kala azar in China, it has rarely been seen in India. DAS GUPTA and SEN GUPTA (p. 468) now report a case in a child in Calcutta, who died in spite of treatment with pentamidoate. They describe the pathological appearances found post mortem.

BRANNACHARI (p. 18) discusses the dermal leishmaniasis which may be found after recovery from kala azar pointing out that it has been recorded only in India. He (p. 550) describes a case of this kind and remarks that although some of these cases respond to antimony others may be completely resistant to it.

SEN GUPTA (p. 17) has continued earlier research on the value of the WITEBSKY KLINGENSTEIN and KURSI antigen in the complement fixation test for kala azar. The results indicate a high degree of specificity even in cases in which the aldehyde test is negative. Positive results may be given in severe leprosy but the test is negative in all the other diseases likely to be considered in differential diagnosis.

Treatment Control

The effect of antimony in kala azar in the opinion of BOIX BARROS (p. 271) is due not to a direct action on the parasite, but to an action on the cells of the reticulo-endothelial system of the host—antimony resistance is a result of failure of this action. Not infrequently the first effect of antimony treatment is the production of a negative phase in which all the symptoms are accentuated, and which is followed by a phase of improvement. The author states that in some cases in which both kala azar and malaria are present, treatment with antimony eradicates both infections.

GOODWIN and PAGE (p. 20) studied the excretion of organic antimonials by means of a polarographic procedure. Much of the antimony is excreted in the urine within a few hours of injection and a large proportion of the pentavalent preparations remains pentavalent but there is evidence that some part is reduced in the body to the trivalent state. Though proof is lacking it may be as generally supposed, that the pentavalent compounds are leishmanicidal only

KIKUTH and SCHMIDT (p 194) describe two preparations of solustibosan. The first is concentrated solustibosan which contains five times as much antimony as the original solution yet is absorbed after intramuscular injection, without irritation. The second is a suspension of solustibosan in oil. This can be injected intramuscularly and is absorbed within 48 hours. The action of the suspension is apparently more continuous than that of the watery solution and cure of kala azar is possible with fewer injections and less antimony. In Spain for children five injections each of 1 cc. per kgm body weight were given at intervals of two days and were well tolerated. Results were good except in severe cases in which a second course was needed. Concentrated solustibosan was also satisfactory when given intramuscularly for kala azar and has also proved successful in the treatment of oriental sore by local injection. These two preparations may constitute a definite advance in the therapy of Mediterranean kala azar and oriental sore. LOZANO MORALES (p 195) and GIL BERMÚDEZ (p 655) also write of the favourable effect of concentrated solustibosan and the oily suspension in the treatment of kala azar. These preparations are of low toxicity and are well tolerated there being neither local nor general reactions.

KORNETOV and MIRZOYAN (p 272) report favourably on solusurmin the Russian equivalent of solustibosan in the infantile kala azar of Central Asia.

GIRAUD and REVOL (p 109) have used an organic antimonial, for the treatment of kala azar which they name pentastib. This is apparently useful but the best drug in their opinion, is urea stilbamine. Pentamidine is useful at the beginning of treatment in young children and in severe cases.

In the treatment of kala azar in East African troops infected in the area near Lake Rudolph COLE (p 831) has found urea stilbamine to be the most successful drug. Stilbamidine was not so effective but the author admits that the dosage employed may have been too low. He places emphasis on the value of blood transfusion especially where secondary anaemia is present with oedema, epistaxis and bleeding from other mucous membranes. Every opportunity must be taken to improve the wasted condition with meat and a diet rich in vitamins.

SOMERS (p 654) gives an account of five patients with the Sudan form of kala azar who responded well to treatment with stilbamidine. Kala azar in the Sudan is notoriously resistant to antimony but although the author admits that the period of observation of these patients is not long it seems that four can be regarded as cured. The fifth showed some abnormalities of the blood when this paper was written.

SÜSKIND and ROTH (p 377) report two cases of kala azar in children in Palestine in which cure was obtained after long-continued treatment with stilbamidine and ROTH (p 551) reports cure of kala azar by 42 intravenous injections of that drug.

SEN GUPTA (p 738) refers to patients with kala azar and tuberculosis, for whom treatment with antimony is contraindicated because its effect on the tuberculous condition is always disastrous. He quotes a case in which the kala azar was cured by treatment with stilbamidine without aggravation of the tuberculous process. This treatment therefore seems to offer a solution of what was at one time an insoluble problem.

The same author (p 273) refers to delayed reactions which have been observed in 17 of 104 cases of Indian kala azar treated with stilbamidine. The neuro-pathic symptoms confined almost entirely to the face first made their appearance 3-4 months after completion of the course of treatment. They consisted of sensory disturbances and dissociated anaesthesia, and there were no nervous lesions elsewhere. The cause of these disturbances is presumably a toxic degeneration in the principal nucleus of the fifth nerve in the pons. The condition shows a tendency to slow recovery.

HENRY (p. 196) has made further observations on the changes which exposure to light makes in solutions of stilbamidine—a subject which had previously been investigated by several other workers. Details should be sought in the original abstract, but the author suggests, on theoretical grounds, that 2-(4-amidino phenyl)-6-amidino indene should be a stable product and might possess all the advantages of stilbamidine as a therapeutic agent. DEVINE (p. 930) describes a colorimetric method of estimating the concentration of stilbamidine by means of which he has shown that in a solution exposed to good window light for two hours about two thirds of the compound are transformed into a derivative which does not respond to the test.

ADAMS (p. 20) reports apparent cure by propamidine in a case of Indian kala azar.

NAPF and SEN GUPTA (p. 18) treated 32 cases of kala azar with pentamidine. 29 were cured but one subsequently relapsed and the authors remark that it is not yet possible to say how many will be permanently cured. Toxic reactions are less severe than those provoked by stilbamidine. In an Editorial in the same journal it is pointed out that in India kala azar usually responds well to pentavalent antimony compounds which do not produce unpleasant symptoms such as those provoked by the aromatic diamidines but that in the Sudan antimony is less successful. SEN GUPTA (p. 736) later followed up 22 of these patients, who were apparently cured by pentamidine. Of these, 12 relapsed and in view of this finding he regards pentamidine as a drug which possesses some degree of curative action but as less useful than stilbamidine and the best of the pentavalent antimonials.

BURKE (p. 469) describes the methods adopted for the control of kala azar in certain tea plantations in Assam. These methods included isolation and treatment of all discovered cases, constant mass surveys by inspection and the application of the aldehyde test and thorough investigation of contacts. If a serious outbreak occurred the infected coohe lines were burnt. Regular spraying of the houses and of the surrounding bush was carried out with a view to destroying the sandfly vector. Cultivation of cleared areas being a potent method of sandfly control, the establishment of gardens was always encouraged.

CUTANEOUS ORIENTAL SORE.

STERNFELD (p. 551) notes that cutaneous leishmaniasis, endemic in Palestine near the Dead Sea and Jericho, has recently spread to Haifa and the northern part of the country.

ELMES and HALL (p. 833) report 10 cases seen at Kano, Nigeria, in which the diagnosis of oriental sore was confirmed by the finding of *L. tropica*. They have therefore proved the accuracy of earlier statements that cutaneous leishmaniasis is found in Nigeria.

DAVEN and AHMED (p. 21) report the occurrence of oriental sore in Hyderabad State.

On epidemiological grounds PARROT and GOUGIS (p. 736) suggest that *Phlebotomus roubaudi* may be a vector of *Leishmania tropica* in parts of French West Africa.

SACHDEV (p. 470) has used local intradermal injections of quinaquine (atebrin) with success in the treatment of oriental sore. Injections are given round the sore until it is completely infiltrated. One series may be enough but it may be necessary to repeat the procedure at weekly intervals.

MUCO-CUTANEOUS (AMERICAN)

McCORD (p. 656) writes of the mucocutaneous leishmaniasis of Yucatan which is contracted by gum collectors who during the rainy season enter the jungle

in the course of their work. There is no precise information as to the actual method of transmission of this disease

PESCE and PARDO (p 110) have found leishmaniasis in several parts of Peru and give information on the sandflies collected in their investigation.

COSTA (p 737) notes that the initial lesion of American muco-cutaneous leishmaniasis occurs on exposed parts of the skin. He quotes a case in which a painless ulcer surrounding the thumb nail was found to contain the parasites

REY (p 110) gives a description of the cellular reactions which take place after subcutaneous injection of cultures of *Leishmania brasiliensis* into hamsters

COSTA (p 1011) reports a case of nasal polypus apparently due to leishmaniasis of the American type

Prognosis in cases of American muco-cutaneous leishmaniasis in which the mucous membranes are severely involved is not good and LUIS CARRI (p 737) urges the importance of treatment when the disease is in the early cutaneous stage. Several forms of treatment are mentioned, which give good results if applied early

PERA CHAVARRIA *et al* (p 551) claim to have treated American muco-cutaneous leishmaniasis successfully by administration of a solution of tartar emetic by the mouth. The initial dose in children is about 1 mgm a day which is increased to the limit of toleration without diarrhoea or vomiting in adults the initial dose is greater. Cure has been obtained in 3-4 months by this method.

Charles Wilcocks

MALARIA.

McCoy O R. Malaria and the War. *Science* 1944 Dec. 15 535-9

This is a paper written in general terms on the enormous part malaria has taken in the present war with a brief account of the drugs now used in cure and prophylaxis and of the other measures which should be adopted for prevention. The final section refers to the possible spread of malaria to areas hitherto free or relatively free from it either by the introduction of the vector mosquitoes or of persons harbouring the infection

Charles Wilcocks

BECKMAN H. Will Returned-Soldier Malaria menace Wisconsin? Reprinted from *Wisconsin Med J* 1944 Dec. 7 pp 2 figs. [19 refs]

There can be no doubt that malaria will be brought to many parts of the U.S.A. including Wisconsin by soldiers returning from malarious countries as the diagnosis of malaria is often difficult the author suggests that a competent malariologist should tour the State of Wisconsin and instruct its physicians in the diagnosis and treatment of the disease

Anopheles quadrimaculatus is present in a large part of the densely populated area of the State and several outbreaks of malaria in recent years have shown that it can transmit malaria in this State. The time of the year when an infected soldier returns will be important if he infects mosquitoes during the early part of the summer malaria may spread but if he only returns in time to infect the last brood of mosquitoes in the autumn it is very unlikely that the infection in the mosquitoes will survive the winter. It is possible that some foreign strains of malaria parasites may not be transmissible by *A. quadrimaculatus* and the fact that this species of mosquito prefers animals to man diminishes the risk of outbreaks of malaria.

The possibility of the introduction of new species of *Anopheles* is more serious, as was shown by the introduction of *A. gambiae* into Brazil. It is unlikely to happen in Wisconsin but precautions against it should be maintained. Prisoners-of-war camps are unlikely to be a danger as mosquito control there is satisfactory. The population of Wisconsin is also protected by its relatively high standard of living and by the fact that most houses are screened. Should an epidemic arise there are ample means of dealing with it successfully. There is no reason to think that malaria will become endemic in Wisconsin. The author gives references for the various points discussed and for support of his conclusions. J F Corson

SHUTE, P G Malaria in England. *Pub Health* 1945 Mar v 58 No 6 62-5

DHICARY B M Malaria in Infants. *Indian Med Gaz* 1944 Dec. v 79 No. 12, 594-5 3 charts.

On a tea estate in Assam during a period of 5 years, records were kept of the incidence of malaria in infants at different ages during their first year of life of the incidence of malaria in these infants in different months of the year and of the monthly rainfall. The object was to determine roughly the good and bad mosquitoes were infective in the field. Of 349 children born during the 5 years 71 became infected during their first year of life the highest number (19) at three months of age the highest incidence (19) in September and the highest rainfall occurred from May to September the peak being in June. J F Corson.

MAXSON BARR P & MUGGLETON W J The Persistence of *Plasmodium ovale* (Merrittanda.) *Brit Med J* 1945 Mar 17 369

A patient had an attack of quartan malaria in Sierra Leone in June 1939 and was treated with plasmoquine compound which however produced plasmoquine poisoning and had to be stopped. A second attack of fever in July was treated adequately with quinine and mepacrine. After a leave in Britain, the patient returned to Sierra Leone in August 1942 and has remained here there, and finally returned to Britain in August 1942 and has remained here since. In December 1942 she had fever which was treated with mepacrine and quinine though no parasites were found. She remained well more or less until March 5th 1944 when she developed high fever (106°F) with headache lumbar pain and vomiting this recurred at 48-hour intervals. When seen on March 16th a fairly heavy infection of half-grown *P. ovale* was found she was treated with mepacrine and quinine and has remained well since.

As a possible explanation of the long persistence of *P. ovale* in this patient, the authors mention SHUTE's theory (this Bulletin 1940 v 37 289) that some of the sporozoites may remain in the tissue cells from the time of the mosquito bite instead of entering the blood stream or there might be an exoerythrocytic cycle like that in bird malaria though it has not yet been demonstrated in man. This case shows that *P. ovale* may cause serious illness with high fever or as the authors have shown (this Bulletin 1937 v 34 585) with symptoms simulating appendicitis. J F Corson

MATTINGLY P F New Keys to the West African Anophelinae. *Ann Trop Med & Parasit* 1944 Dec. 30 v 38, Nos. 3 & 4 189-200 2 figs. [17 refs.] Since the publication of Leeson's keys to the larvae and adults of West African anophelines [this Bulletin 1939 v 36 810] five species have been added

to the known anopheline fauna of that region. Three of these are recorded for the first time in West Africa, in the paper under review *Anopheles implexus leeson* and *rivulorum*. The key also includes larval characters of *Anopheles flavicosta* and *wellcomei* which had not been described at the time when Leeson's key was published and larval and adult characters of *A. marshalli theileri* var *brohieri* and *obscurus* var *nomini* which were not included by Leeson. Characters are also included for separating *Anopheles constanti obscurus rufipes* and *gambiae* from their varieties.

Larvae of *Anopheles rivulorum* and *leeson* are recorded as having been collected from the Oshun and Ennle Rivers near Oshogbo and in the Oyo Province all in Southern Nigeria. *A. leeson* has also been recorded from Northern Nigeria. *Anopheles implexus* is recorded from the highlands of the Gold Coast. [No condensation of the real subject is possible. The keys will be found of great use to all workers in this field.] G Macdonald

EYLES D E A Critical Review of the Literature relating to the Flight and Dispersion Habits of Anopheline Mosquitoes. *Pub Health Bull No 287* Wash 1944 39 pp [Bibliography]

The length of flight of anophelines determines the radius of control needed around habitations and as the cost depends on the area to be controlled which varies with the square of the radius it is of great practical importance to measure it accurately and not adhere to generalizations which may involve either excessive cost or ineffective control.

It is important to differentiate between the maximum range of flight and the effective range at which disease is commonly transmitted, usually less than the maximum. The flight varies greatly in different species and under different conditions. For each species there is an ordinary flight between breeding place and the source of blood in some species such as *A. maculipennis* there may be also a seasonal flight associated with hibernation up to a radius of nearly nine miles and in any species dispersion may be increased by very prolific breeding, absence of nearby sources of blood favourable winds or artificial means such as vehicular traffic.

Experimental study is by the liberation of marked mosquitoes. The original method of marking by spraying mosquitoes with a solution of dye has been superseded by the use of metallic powders such as aluminium or gold stripings containing a proportion of minute particles which adhere to the insect without causing it harm. Advance has also been made in the field marking of mosquitoes in the larval stage by the addition of Giemsa and other stains to the water though this method is subject to the disadvantage that subsequent detection is very slow.

Experimental insects may be marked by applying the dye or dust on wild mosquitoes in their natural resting places or by marking and releasing artificially reared adults near a natural breeding place or by marking wild adults captured for the purpose and again released. It is important to ensure that they are released near the site of capture as disorientation may affect the length of flight. Most of the observations however have been based on an estimate of the distance of the nearest breeding place from the site of capture of wild adults a method which is open to several fallacies.

All available evidence on the flight range of different species of anophelines has been collected and it is summarized in this paper in a form which should be consulted in the original by all interested. The flight range of the important anopheline vectors is tabulated as follows —

TABLE I—A Tabular Summary of the Data Available on the Flight Range of the Important Anopheles Vectors.

	Maximum observed flight range	Maximum flight proved by experiment	Maximum noted seasonal flight
<i>A. albimanus</i>	1.0 mi. (LePrince 1917) 0.5 mi. (Christophers, 1904)	117 mi. (Zetek, 1915) 0.31 mi. (Atkins et al. 1940)	12 mi. (Curry 1934).
<i>A. culicifacies</i>	0.11 mi. (Davis & Humm, 1932)	—	—
<i>A. darlingi</i>	0.5 mi. (Stephens & Christophers, 1907)	—	—
<i>A. fluviatilis</i>	4.5 mi. (DeMeillon, 1933)	4.5 mi. (Adams, 1940)	—
<i>A. forestus</i>	3.0 mi. (Symes, 1930)	4.25 mi. (Adams, 1940)	—
<i>A. gambiae</i>	0.5 mi. (Watson, 1933)	1.38 mi. (Wallace, 1940)	—
<i>A. maculipes</i>	6.5 mi. (Demokidov 1925)	4.58 mi. (Ottoleang et al. 1928)	11.25 mi. (Shipova, 1938)
<i>A. maculipennis</i>	5.6 mi. (Swellen-grebel & Nyk amp 1934)	8.7 mi. (Swellen-grebel & Nyk amp, 1934)	—
<i>A. maculipennis atroparvus</i>	1.0 mi. (Harrison & Ramsey 1933)	—	8.0 mi. (Manson & Ramsey 1933)
<i>A. merus</i>	2.5 mi. (Craig, 1909)	1.5 mi. (Russell & Santiago 1934b)	—
<i>A. merus flavescens</i>	8.0 mi. (Kirkpatrick, 1925)	—	—
<i>A. multicolor</i>	—	3.7 mi. (Rockard, 1928)	—
<i>A. parafurcata</i>	1.75 mi. (Smulhe, 1876)	2.5 mi. (Evles & Bishop, 1943)	—
<i>A. quadrimaculatus</i>	2.8 mi. (Kluger, 1941)	—	8.7 mi. (Kluger & Mer 1930)
<i>A. sacharovi</i>	1.53 mi. (Kluger, 1924)	—	3.7 mi. (Kluger 1928)
<i>A. sergenti</i>	1.5 mi. (Afendi & Majid 1938)	—	—
<i>A. stephensi</i>	2.8 mi. (Schuurman et al. 1929)	4.0 mi. (van Bree-man 1920)	—
<i>A. sinensis</i>	4.3 mi. (Shawroh, 1927)	—	Mentioned as occurring (Shawroh, 1927)
<i>A. superpictus</i>	—	—	—
<i>A. umbrosus</i>	—	—	—

* This observation was made during a study of a subject other than flight range but was the only reference found to this species.

[This important paper consolidates our knowledge and at the same time reveals the many deficiencies in it. It should form a basis for much further work on this subject.]

G. Macdonald

REEVES W C Preliminary Studies on the Feeding Habits of Pacific Coast Anophelines. *J Nat Malaria Soc Tallahassee Fla* 1944 Dec. v 3 No. 4 261-6 [23 refs]

Precipitin tests have been run on blood from the stomachs of freshly engorged *Anopheles maculipennis freeborni*, *Anopheles pseudopunctipennis* and *Anopheles punctipennis* collected in the field from various parts of the Pacific Coast area of the United States.

Tests were run on 473 smears from *Anopheles maculipennis freeborni* and 3.0 per cent. of this group had fed on man. The highest rate for any single area was 7.1 per cent. positive to human blood.

From *Anopheles pseudopunctipennis* 178 smears were tested with 0.6 per cent. having fed on man.

For *Anopheles punctipennis* 52 smears were tested of which 3.8 per cent. had fed on man.

YOLLES T K YOLLES S F & BYRD D A On the Occurrence of *Anopheles pessoai* in Trinidad, B W.I. *Science* 1944 Dec. 15 547-8

Anopheles pessoai has been found in Trinidad and there is a strong indication that it was introduced there by aeroplane from the South American continent. Little is known of the ability of *A. pessoai* to transmit malaria, but the importance of this finding is rather that it shows the danger of the introduction of *A. darlingi* by the same means. The distribution of the two species coincides in some areas. *A. darlingi* is a known dangerous vector where it occurs.

Charles Wilcocks

BURGESS R. W & YOUNG M D Methods of Handling and Feeding *Anopheles quadrimaculatus* Say upon Malarious Patients. *J Nat Malaria Soc Tallahassee Fla* 1944 Dec. v 3 No 4 241-7 3 figs

In 1943 the authors reared 100 000 specimens of *A. quadrimaculatus* in their insectarium and 14 000 were infected with malaria by feeding them on malaria patients.

The insects were housed in small glass cages each mosquito having its own cage. The cages are figured diagrammatically. Optimum blood feeding was obtained between 50 and 72 hours after emergence provided that the mosquitoes were given a feed of sugar solution 12 hours or more previously. The authors found that mosquitoes pre-fed on sugar solutions took blood more readily and lived longer than those not pre-fed. Females exposed to mating fed better than virgins—84 per cent of the former and 58 per cent of the latter. Also the mortality was slightly higher among the virgins. [Presumably the spermathecae were not dissected for confirmation of fertilization.]

No appreciable difference was found as regards willingness to feed within variations of temperature ranging between 68°F and 90°F. The mosquitoes fed more readily when they were held on a patient screened from the light. Covering the jars containing the mosquitoes increased the feeding on the light side of the room by 9 per cent. but only by 1 per cent. on the dark side.

In some trials 95 per cent. fed in 5 minutes. [The authors do not state whether they consider this to be due to the type of patient or to some external conditions which stimulate the mosquitoes to feed.] After the mosquitoes had taken an infected blood meal they were kept in an insectarium where both temperature and humidity were controlled. Until the mosquitoes were killed for dissection they were fed on a syrup solution.

P G Shute

FERGIMAN D G Diagnosis of Malaria in West Africa. Brit. Med J 1945 Mar 10 328-30

This paper is based on experience of more than 2,000 cases of malaria in white personnel at an R.A.F. hospital in West Africa nearly all *P. falciparum* infections. The vast majority of patients had never been exposed to malaria infection before arrival in West Africa where their stay had been temperatively short. Drug suppression (mepacrine 0.2 gm. twice a week) and antimalaria discipline were enforced. Pernicious cases were uncommon there were nine cases of blackwater fever four of cerebral malaria and one of choleraic type all recovered. There was no algid case and chronic malaria was very rare. Parasites are not always found in the blood. A description is given of the symptoms that have been helpful in diagnosis in the absence of positive blood findings. For routine purposes a temperature of 103°F was taken as a dividing line between seriously and not so seriously ill cases. Seriously ill cases were treated at once unless the symptoms indicated a definitely non-malarial disease. In the great majority of low fever cases it was possible to arrive at a shrewd diagnosis within 48 hours.

In 136 consecutive low fever suspected malaria cases immediate treatment was withheld. Blood slides were examined on admission and then night and morning. Parasites were found in 90 of these patients—in 66 in the first slide in 14 more within 24 hours, and in six more within 48 hours. Tenderness of the spleen was first seen after longer intervals.

Of the clinical features assisting diagnosis splenomegaly was important in 25 per cent. of 406 consecutive patients had splenic enlargement as compared with about 5 per cent. of the personnel outside hospital. Tenderness of the spleen was almost pathognomonic and tenderness under the left costal margin, in the absence of a palpable spleen, was of great diagnostic value. Some or all of the common early constitutional symptoms—headache backache aching limbs dry cough, vomiting, fever splenomegaly and herpes—were noted alone in 83 per cent. of 345 consecutive cases, coryza or productive cough in 9 per cent. simple diarrhoea in 4.5 per cent. and dysentery in 0.75 per cent.

Subclinical malaria was not uncommon in ambulant members of the staff. Recurrent headache was the chief complaint sometimes backache, aching limbs and malaise. Antimalarial treatment produced a sense of well being. The incidence was about 10 per cent. of the total strength. Blood slides were usually negative. The absence of anaemia, and the general condition, did not justify a diagnosis of chronic malaria and latent malaria suggests the absence of all symptoms.

Treatment of malaria was continued for twice as long as the pyrexial period, with a minimum of seven days. Mepacrine 0.1 gm. three daily was given for a maximum of 10 days it was then replaced by quinine 10 grains twice daily. If longer treatment was indicated. For the first two or three days quinine, 10 grains thrice daily was given in addition to the mepacrine. The ambulant cases of subclinical malaria were given mepacrine 0.1 gm. and quinine five grains daily for two weeks, and then mepacrine 0.1 gm. for six days a week, either temporarily or permanently.

Norman White

MARSHALL, J M Spontaneous Rupture of the Malarial Spleen. U.S. Nav. Med. Bull. 1944 Oct. v 43 No 4 743-7

A Marine corporal, home on leave had a dull, generalized aching pain in the abdomen. He stayed quiet but six hours later he had severe abdominal pain and vomited once. A doctor was called who gave a hypodermic injection of hyoscine grain 1/100 morphine grain 1/60 and caustic grain 1/60 (presumably a

preparation of *Cereus grandiflorus*] The injection was repeated in an hour because of the persistence of severe pain and the patient was taken by ambulance to a hospital 25 miles away

On admission the patient was acutely ill. His blood pressure was 125/75 pulse rate 120 temperature 97.8°F and respirations 20 per minute. He appeared to have a perforated abdominal viscus and immediate laparotomy was performed approximately 10 hours after onset of the initial symptoms. Free blood was found in the abdomen and a greatly enlarged spleen was the source of bleeding. The large purple spleen 25 by 15 by 8 cm. was ruptured transversely through the middle but the capsule was intact on the pedicle side. A triangular fragment of spleen 6 by 8 by 10 cm. had become completely detached from the border of the fracture line and was floating free in the abdominal cavity which contained at least 1000 cc. of blood. The spleen was removed. The peritoneal cavity was washed out with warm saline and 5 gm. of crystalline sulphanilamide were instilled into the splenic fossa. The wounds were closed without drainage. Blood transfusions were given. The patient left hospital four weeks after operation in good condition. An attack of *P. vivax* malaria was the only complication of convalescence.

There was no history of trauma in this patient. He had had 14 attacks of malaria during the preceding twelve months, nine of which had been spent in the south west Pacific.

The diagnosis of intraperitoneal bleeding is not always easy. In patients who have or who have had malaria and in whom an acute abdominal emergency develops spontaneous rupture of the spleen must be considered as one of the possibilities. Immediate splenectomy is the only treatment. Whole blood or plasma should be administered promptly to compensate for the loss of blood.

Norman White

WATERMAN J. A. Cases of Malarial Nephritis or Nephrosis. *Caribbean Med J* 1944 v 6 No 5 359-60

ROBERTSON J. N. Ophthalmologic Lesions encountered in Tropics, with special reference to Ocular Manifestations of Malaria. *North Carolina Med J* Winston Salem. 1944 Oct. v 5 483 [Summary taken from *J Amer Med Ass* 1944 Dec. 23 v 126 No 17 1118.]

According to Robertson optic neuritis and amblyopia are at times associated with malaria. The amblyopia has to be differentiated from that which is due to quinine. In quinine amblyopia the condition depends on the retinal anemia resulting from the toxic spasm of the arterioles. There is extreme pallor of the optic disks and contraction of the visual fields. This picture is in direct contrast to the hyperemic disk and retina associated with malarial toxemia.

Malarial amblyopia occurs as a result of the action of the malarial toxin on the optic nerve and retina. Often optic neuritis and papillary edema result from the blocking of the retinal and choroidal vessels by parasites and leukocytes. The retinal hemorrhages are usually small multiple and peripheral. Large macular hemorrhages do occur in the malignant types of malaria. Ulceration of the cornea is the most common ocular sequela of malaria and recurrent iritis is frequently associated with this keratitis. Supraorbital neuralgia precedes the corneal lesions. Photophobia and lacrimation are characteristic signs and often precede the corneal lesions by days or weeks. On an island in the Southwest Pacific the author encountered many patients with intraocular disturbance among men between the ages of 20 and 30. Many had suffered some depletion of the powers of accommodation and convergence as was manifested by the complaints of reading difficulties, scotomas and muscle unbalance particularly

[June 1945]

exophthalmos. Subjectively the complaints were loss of vision, frequent headaches in the occipital and temporal regions, dizziness, pain in the eyeballs, tenderness on palpation, photophobia, lacrimation and spots before the eyes. The objective findings were irregularity of the pupils, retinitis of the atrophic type, usually in or around the macular area, unusual concentration of choroidal pigmentation, generalized hyperemia of the retina and nerve head, optic neuritis both mild and severe, optic atrophy and in a few cases a severe progressive choroidoretinitis and uveitis. Some of the patients who were evacuated were followed up by the author since his return. Some of them now have a chronic uveitis."

ROSENBERG, A. A. Effect of Malaria on Serologic Tests for Syphilis. *Bull. U.S. Army Med. Dept.* 1945 Jan., No. 84 74-80. 23 refs.

After discussing the incidence of false positive reactions in malaria (with numerous references) in various types of tests for syphilis, the author describes a study which he carried out.

His objects were

- (i) to determine which test gave the smallest number of false positive reactions, and
- (ii) to discover whether it was possible to distinguish malaria from syphilis on the basis of definite patterns of positivity among the different tests.

The tests chosen were the standard flocculation tests of Kahn, Mazzini, Eagle, Hinton and Kline and the standard complement fixation test of Kolmer; all antigens used were approved by the authors of the respective tests and the published techniques were followed in detail. Blood was obtained from patients with positive smears for plasmodia at certain intervals: 1-4 days, 7-10 days, and 12-30 days. The malaria infections were grouped as *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae* and *Plasmodium ovale*. Results are shown in the following table—

Species of parasite	Percent total area	Percentage of positives				
		Kahn	Kolmer	Mazzini	Eagle	Hinton
<i>Falciparum</i>	20	43	23	52	15	9
<i>Vivax</i>	70	48	71	51	9	3
<i>Falciparum</i> and <i>Vivax</i>	"	70	52	87	29	17
Not classified	8	37	17	47	47	10

From this it will be seen that the Hinton test gave the smallest number of false positive reactions, and that double infections gave more false positives than single ones.

The author constructed a second table from the above showing expected incidence of false positive reactions in the general malaria population in the particular locality surveyed in the present report. This gives the following percentages: Mazzini 51.0 Kahn 47.5 Kline 33.8 Kolmer 20.4 Eagle 10.4 and Hinton 5.8.

The following clinical observations were made. The strongest false positive reactions occurred 7-10 days after the chill, and they persisted for 4-6 weeks. Reactions remained positive longer in *P. falciparum* infections. When there was a recrudescence of the malaria the tests became stronger or remained at a high

level the serologic reaction was not influenced by the stage in the life-cycle of the parasite at the relevant time. Fever was not the cause of the positive reactions and these latter were not affected by the antimalarial remedies mepacrine, pamaquin or quinine.

The author attempted to discover whether malaria could be distinguished from syphilis by the results of serum tests. In malaria the Kahn and newer Mazzini tests were generally 3+ or 4+ the Kolmer \pm or +. The Kline varied from \pm or + to 2+ or 3+ when the Eagle or Hinton tests were positive they quickly reverted to negative. The Hinton test was the most sensitive in cases of syphilis in malaria cases there were only 2.3 per cent. 4+ Kolmer reactions whereas in syphilis in this age group 40 per cent. would be expected when malaria was coincident with syphilis all tests became stronger during the malaria attack but after four weeks the original pattern was restored. In such cases if malaria is present syphilis can almost certainly be excluded if the Hinton test is negative.

Divergent results of tests of malarial bloods are probably due to variations in technique introduced by serologists and to differences in the antigens much also depends on the time when the blood is taken relative to the finding of parasites.

It is concluded that

- (i) Of all generally accepted tests the Hinton yields the smallest percentage of false positive reactions in malaria.
- (ii) Malaria can often be distinguished from syphilis by the pattern of positivity of tests.
- (iii) Persistence of positive reactions beyond six weeks in the absence of continued malarial infection, should arouse a suspicion of syphilis.

T. E. Osmond

MAVEETY H. M., TURNBULL R. B. Jr & BAUER C. R. Kodachrome Photomicrography in Malaria. Rapid Method of Instruction. *U.S. Nav. Med. Bull.* 1945 Jan. v. 44 No 1 134-41 3 figs.

Lantern slides made by colour photography from stained blood films are very useful for class instruction in the recognition of malarial parasites in circumstances where few microscopes are available and the pupils are unfamiliar with microscopical methods and where rapid instruction is necessary. The technique is simple and can be used by any good amateur photographer. The equipment comprises a microscope, a standard Burton light source (100 watts), a Leica camera and Eastman Kodachrome film 35 mm. in rolls of 18 exposures. This film should be of the artificial light type A indoor. A white substage condenser is used and a compensating filter (Eastman Kodak Company) to eliminate the green tint in the transparency. The light source is 8.5 cm. from the concave mirror of the microscope and the photographic film is 20 cm. from the 10x eyepiece. An oil immersion objective is used. Exposures of $\frac{1}{4}$ to 1 second are suitable. The arrangement is shown in diagrams.

Wright's stain was found to be unsatisfactory because the eosin in it causes the red or pink of the blood film to have a greenish tint in the photograph. The following modification of Giemsa's stain was found satisfactory. Giemsa stain 1 part, Giemsa buffer solution 10 parts, methylene blue solution (1:10,000) 0.4 part. Stain for 40 minutes. [GIEMSA (*Misch med. Week.* 1935 v. 82 1076) stated that he used Weise's buffer solution (this *Bulletin* 1933 v. 30 727). Weise found a buffered water of pH 7.2 the best for diluting Giemsa's stain. It contained potassium phosphate of Soerensen (KH_2PO_4) 0.49 gm. and sodium phosphate of Soerensen (Na_2HPO_4) 1.14 gm. per litre. For showing Schuffner's, Maurer's (Stephens & Christophers) and Ziemann's dots he raised

the pH to 7.5 by adding to this solution 20 cc. of 1/10 N (25 drops of 10 per cent.) NaOH solution to the litre.]

J. F. Corson.

GREEN, R. A. Totaquine in the Treatment of Malaria. *Bull. U.S. Army Med. Dept.* 1945 Jan. No. 84 51-7 2 charts.

In a foreign theatre of war a controlled study was made of the relative efficacy of totaquine, quinine and atabrine (mepacrine) respectively in the treatment of malaria. During a period of 11 weeks, 304 cases of malaria were admitted to hospital. The total strength of the battalion concerned was only 511 so the admission rate was 2,814 per thousand per annum. Only 165 individuals were affected, 112 of whom relapsed once and 27 twice. Of the initial attacks 131 were due to *P. vivax*, 15 to *P. falciparum* and 19 to mixed infection. *P. vivax* was found in all relapsing cases. Only one death occurred in the series: the patient had a spontaneous rupture of the spleen on the second day of his first relapse; the initial attack had been treated with quinine.

The first 240 cases were treated in rotation with either totaquine or quinine or atabrine, 80 cases with each. The doses of totaquine and of quinine employed were 1 gm. thrice daily after meals for two days, then 0.6 gm. thrice daily for five days. The doses of atabrine were 0.2 gm. every 6 hours for five doses, then 0.1 gm. thrice daily for six days. The composition of the totaquine used was

	Per cent.
Cinchonine	29.0
Quinine	9.6
Cinchonidine	31.2
Quinidine	5.3
Anhydrous quinine	9.6
Total anhydrous crystallizable cinchona alkaloids	73.0

The average duration of persistence of parasites in the blood after the commencement of treatment was with totaquine 2.73 days, with quinine 2.53 days and with atabrine 2.25 days. The duration of fever was with totaquine 2.2 days, with quinine 2.25 days and with atabrine 2.7 days. The incidence of toxic symptoms caused by totaquine and quinine was about equal but the nausea and vomiting caused by totaquine were more disagreeable than any effects due to either quinine or atabrine. Of the cases treated with totaquine, 65 per cent. relapsed, with quinine 70 per cent. and with atabrine 38.7 per cent.—all during the 11 weeks period of observation. The period between initial attack and relapse was three times as long after atabrine treatment as it was after quinine or totaquine treatment.

Norman White

HEILIG, R. & VISVESWAR, S. K. The Influence of Intravenous Injections of Quinine on the Myocardium. *Indian Med. Gaz.* 1944 Nov v 79 No. 11 514-18, 2 figs. on pl. No. 24 [27 refs.]

A review of the literature is given. RAO & NAIDU (*Quart. Bull. Mysore Med. Ass.*, 1943 v 7 105) found that clinical observation could detect no ill effects after single doses of quinine dihydrochloride not exceeding 10 grains injected slowly in proper dilution. In the present investigations 24 patients with uncomplicated malaria were given a total dosage of 40 grains of quinine dihydrochloride divided into five intravenous injections (5, 7, 8, 10, 10 grains) on five consecutive days. Each dose was dissolved in 10 cc. of water. After the fifth injection, 14 patients (in eight of whom the electrocardiogram had previously been normal) showed definite signs of myocardial impairment. In six of them, the damage was considerable. [For the technical details, the original should be consulted.] Systolic and diastolic blood pressures were reduced by 10-15

mm. Hg in all the patients after the third dose but the reduction was not increased by subsequent doses. This diminution of blood pressure is believed to be due to an effect on the peripheral blood vessels. It is concluded that quinine should not be injected intravenously unless there is specific indication for this method of administration.

F Hawking

HARNED B. K & ETTELDORF J. N. The Concomitant Administration of Sulfathiazole and Quinine or Atabrine. *Amer J Med Sci* 1944 Dec. v 208 No 8 750-56 2 figs

The effect of giving sulphathiazole simultaneously with mepacrine or quinine was investigated in 99 patients. The highest doses given were sulphathiazole 6 gm daily for seven days, quinine bisulphate 2 gm. daily for seven days and mepacrine 0.3 gm daily for five days. With the possible exception of vomiting these combinations of drugs did not cause any more adverse symptoms than those following any of the compounds separately. The combination of drugs produced no changes in the haemoglobin percentage or total white cell count of the blood. Quinine and mepacrine produced only minor changes in the free and total sulphathiazole in the blood and urine.

F Hawking

BARLOW O. W. AUERBACH M. E. & RIVENBURG H. Studies of the Pharmacology of Atabrine on Mice, Rats, Ducks, and Dogs. *J Lab & Clin Med* 1945 Jan. v 30 No 1 20-31 5 figs [16 refs]

Various useful chemical and physical data are given about eight salts of mepacrine (atabrine). In mice the LD50 of mepacrine dihydrochloride given by mouth is 0.706 gm. per kgm. and when given intravenously 0.02 gm. per kgm. Mepacrine was made by various combinations of American or German materials by American or German methods. When given by mouth to young rats the toxicity of the different preparations were indistinguishable (LD50 0.615-0.670 gm. per kgm). Similarly when given to dogs the three different preparations used were indistinguishable in their effects. Twenty five mgm. mepacrine per kgm. were given each day for three days and the dogs were killed on the fourth day. The average concentration of mepacrine dihydrochloride in the different organs was heart 4.0 mgm per 100 gm., lungs 13.1 mgm., liver 31.7 mgm., spleen 18.8 mgm. and kidneys 7.9 mgm. Altogether 17 per cent. of the total dose was recovered. When fed in a mash to ducks the American product was slightly less toxic than the products made from German intermediates. When a single dose of 675 mgm. per kgm. was given orally to rats the concentration in the spleen was greatest at 24 hours afterwards (0.22 mgm. per gm.) and that in the liver at 8 hours (0.16 mgm. per gm.). In other experiments it was shown that a significant blood concentration was maintained in rats as long as mepacrine deposits existed in the liver.

In rats given daily 5 per cent. or less of the LD60 no pathological changes were found in the viscera. But in rats given 10 per cent. or more of the LD60 there were large necrotic areas in the liver, the mepacrine content of these areas was not greater than that of the normal liver tissue. The kidneys, adrenals, spleen and heart were enlarged and all the viscera were stained deep yellow. No significant changes occurred in the red blood cell or white blood cell counts or in the haemoglobin values. Mepacrine did not retard the growth of young rats unless the daily oral dose was at least 45 mgm per kgm.

F Hawking

LEWIS R. A. A Simple Method for estimating Serum Atabrine Concentration. *J Lab & Clin Med* 1944 Dec. v 29 No 12 1303-6.

Fifteen cubic centimetres of blood are placed in a 15 cc. centrifuge tube. After the blood has clotted it is ringed with a glass rod and centrifuged for

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HODGKINS J A ROSE A S. TRACY L D & PROUT C. The Effect of Penicillin on Inoculation Malaria. A Negative Report. New England J of Med 1945 Feb 1 v 232, No 5 133-8 3 figs.

"During investigations on the use of penicillin in neurosyphilis 28 patients received both penicillin and benign tertian malaria. Fifteen of these had penicillin administered simultaneously with the malaria. Clinical charts of nine cases are presented. These charts graphically demonstrate that penicillin does not suppress fever or the parasite count of active inoculation malaria and that when given before or at the time of the malaria inoculation it does not prevent or postpone the development of fever and parasitemia.

It is reasoned by analogy to known antimalarial drugs that since penicillin does not have an antimalarial effect on inoculation Plasmodium vivax malaria, it will not be effective in other types of malaria or in naturally acquired malaria. Since the writing of this paper we have had further experience in the use of penicillin in therapeutic malaria. In view of the fact that penicillin is rapidly removed from the body we have tried more frequent injections to exclude this possible loophole in the ineffectiveness of the drug. We have given 3 000 000 units in five days at the rate of 50 000 units at each intramuscular injection every two hours, day and night. This method has been used in about 20 cases without any change in the paroxysms of fever or in the parasitemia.

BRADLEY G H. The Entomological Phases of Malaria Control Programs. J Nat Malaria Soc Tallahassee Fla. 1944 Dec v 3 No 4 249-53

The paper briefly summarizes the history of the attack on anophelines in the Northern American continent starting from Howard's paper in 1900 on mosquitoes of the United States and coming up to the present time. The principle of species-sanitation was evolved in Panama in 1910 but did not receive general acceptance until 1937 when a number of boards of health employed entomologists. The need for skilled entomological advice became more apparent with the outbreak of the present war and a number of new appointments were made.

A brief account is given of the technique of organization of anopheline control, the determination of the locally important anopheline vectors, the methods of malaria survey, and the checking of control measures.

G Macdonald

STUMPS T H. Educational Factors in the Ultimate Control of Malaria. J Nat Malaria Soc Tallahassee Fla 1944 Dec v 3 No 4 255-9 2 figs.

The efforts of health agencies to prevent malaria are impeded by various individual and public activities such as agricultural customs, water impoundments for industry and commerce, and highway construction and it is the place of education to remove these impediments. Funds for malaria prevention are a legitimate overhead expense of enterprise, and will become more so as malaria declines and becomes a potential rather than an actual risk when the money from public funds to prevent its recrudescence will inevitably decrease and it is the greatest educational task of the malariologist to translate this abstract statement into practical action. Education in the form of professional and technical training, as well as public education through regular channels and the supply of information to the public can convert those agencies which have acted as impediments into assistants in the campaign.

G Macdonald.

GARNHAM P. C. C. & HARPER J. O. The Control of Rural Malaria by Pyrethrum Dusting. *East African Med J* 1944 Oct v 21 No 10 310-20 1 fig

The experiment described was carried out in two villages Ivona and Igunga in the Maragoli District of North Kavirondo in the Nyanza Province of Kenya. The villages are about a mile apart and separated by a valley. Maragoli is on the Equator some 5 000 feet above sea level. It is densely populated over 500 to the square mile by a tribe of the Bantu group which has a fair degree of natural resistance to malaria. The dwellings are the usual round single roomed mud and pole structures with thatched roofs. The hut is sometimes subdivided into stocks being kept in one half. Smoke-grimed walls from fires constantly smouldering and the absence of windows make the interiors dark. Epidemics of *falciparum* malaria occur in the long rains. At other seasons only occasional infections occur. *P. vivax* is rare. Fifty huts in each of the two villages were selected. Those in Igunga were dusted with pyrethrum powder twice a week. The Ivona huts acted as a control. he powder was blown from a distributor and directed chiefly towards the roof. From April to October 1942 the amount of powder used was 1 ounce per 1 000 cubic feet. The smaller dose had little effect. The use of the larger dose was followed by a fall in the parasite rate of children whereas the rate increased in the control village. The dusting appeared to cause a 50 per cent. reduction in the incidence of malaria. No other control measures were employed. Quartan malaria was present throughout the year and at all ages in about 10 per cent. of the children examined. *P. vivax* was found only in August. *P. falciparum* infections increased in June to reach a maximum in August.

A Haddow hut was constructed in each village and searched daily for mosquitoes. Ten ordinary untreated huts in each village were also searched twice a week. The two vector species *A. gambiae* and *A. funestus* were four or five times more numerous in the treated than in the untreated village. The *A. gambiae* season begins first with the long rains and is overtaken three months later by *A. funestus* and later still by *A. marshalli*. *A. funestus* was practically absent in 1943 as in many other parts of Kenya that year. *A. marshalli* was a common domestic mosquito but does not appear to be a malaria vector. no sporozoites were found in 485 dissected at a season when the *A. funestus* sporozoite rate was 2 per cent. Of other mosquitoes found in huts were small numbers of the following *Aedes* species: *A. aegypti*, *A. metallicus*, *A. africanus*, *A. longipalpis* and *A. ingrami*. The last three being tree-hole breeders. A microfilaria was found in the blood of 18 per cent of the children. Its vector appeared to be *Culicoides trichopsis* and its morphology resembled that of *Acanthocheilonema persians*.

Norman White

HÖHNE W. Malariasanierung in Chalkis. Ein Beispiel für die Spätsommer Sanierung der Anophelenbrutplätze in einer von deutschen Truppen besetzten griechischen Stadt. [*Malaria Control in Chaleis (Greece)*] *Deut Militärarz* 1943 July v 8 No 7 371-6 7 figs

A survey of mosquito breeding grounds in and round Chalcis is described in general terms. The paper is well illustrated by seven maps. The intention of the author obviously is to call the attention of his fellow medical officers to the possibility of carrying out larval control in certain regions under military occupation. He points out that in the German army chief reliance is placed on drug prophylaxis whereas the British have attached a good deal of importance to mosquito-control measures. Paris green is stated to have been used but little other information is given with regard to the methods or results of the control measures.

John H. D. Mason

ALVARADO C. A. & PERA, L. S. Aplicación de sífonos antilarvarios en la República Argentina. [The Use of Anti-larval Siphons in Argentina.] *Bolet. Oficina Sanitaria Panamericana*, 1944 Oct. v 23 No. 10 878-88, 6 figs.

PATEL, B. V. Thiazole Derivatives of Sulphanilamides in Monkey Malaria. *Quart. J. Pharm. & Pharmacol.* 1944 Oct. Dec. v 17 No 4 297-301 (13 refs.)

Numerous reports have appeared on the activity of sulphonamides in simian malaria [this *Bulletin* 1938, v 35 897 and 900 1939 v 36 824 and 1012, and subsequently]. The present investigation deals with the therapeutic effect of three thiazole derivatives on *P. knowlesi* infections in *Macaca* monkeys. I N⁴-methyl-sulphathiazole II 2-N-sulphanilamido-5-ethylthiazole, and III 2-N-sulphanilamido-5-isopropylthiazole. In all, 12 monkeys weighing between 2½ and 3½ kgm were treated. The drugs were given orally by stomach tube in tragacanth suspension, in doses of 0.5 or 1.0 gm. Sometimes only a single dose and not more than a total of five, were given, dosage being carried out once or twice a day. If parasites disappeared from blood and were absent for more than three weeks, the usual tests for radical cure were carried out. The concentrations of each drug in the free and conjugated form in the blood were determined, and were very low in the case of uncombined drug, rarely exceeding 2.0 mgm. per cent. Toxic symptoms were not noted in the animals. Relapses occurred with drug I after a total dosage of 2 gm. In the case of drug II a dose of 0.5 gm. caused the parasites to disappear temporarily and radical cures were effected in two monkeys which received 2.0 and 5.0 gm. respectively. Four monkeys treated with drug III in doses of from 0.5-3.0 gm. were all radically cured.

J. D. Fulton

SILVERMAN M. CEITHAMER, J. TALLAFERRO L. G. & EVANS E. A., Jr. The *In Vitro* Metabolism of *Plasmodium gallinaceum*. *J. Infect. Dis.* 1944 Nov. Dec. v 75 No 3 212-30 7 figs. (Refs. in footnotes.)

Following the experiments of CHRISTOPHERS and FULTON (this *Bulletin* 1938, v 35 709 and 711 1940 v 37 190 and 509) on the respiratory metabolism of *P. knowlesi* reports by other workers in this field have appeared [this *Bulletin* 1942, v 39 397 and 742 1943 v 40 674]. The object of the present investigation was to study the metabolic characters of *P. gallinaceum* and to relate them to the effects of antimalarial drugs. Since the presence of the nucleated red cells of chickens is an added complication in interpreting results suitable controls have been used throughout the experiments, which for simplicity have been carried out in buffered Ca free phosphate saline aerobically and in Ca free bicarbonate saline anaerobically in the absence of plasma. The manometric measurements were made at 40°C. Before withdrawal of the parafilm blood from chickens by cardiac puncture counts were made of the cells present, including reticulocytes in smears of blood from the saphenous vein. The drawn blood was citrated, and after dilution in the appropriate buffer the cells were washed twice in the same medium resuspended and the cells again counted. It was shown that different oxygen tensions had little effect on respiration. A direct correlation was found between parasitic surface area and metabolic activity in this asynchronous infection. Based on surface area, it was found that parasite respiration and glucose utilization was about seventy times that of normal red cells. The R.Q. of normal red cells was approximately 1 they formed lactic acid, and the carbon balance was in agreement with the glucose used. In the case of parasitized cells, the value of the R.Q. was nearly the same but the carbon balance suggested that some product other than CO₂ and lactic acid was being formed, besides the traces of pyruvic and succinic acids detected.

The parasite can apparently oxidize lactate and pyruvate completely. At pH 7.8 parasite respiration was greatest. In order to find out if CO_2 was assimilated by the parasite (a fact established for a number of microorganisms in recent years) a tracer method was used with sodium bicarbonate as the source of radioactive carbon. With glucose as substrate the result in one of four experiments was positive. In the case of parasitized cells CO_2 and lactic acid were formed from glucose anaerobically.

During the *in vitro* experiments with quinine the distribution of this substance between normal and infected red cells was determined. It was much higher than occurs *in vivo* after administration of the drug and is probably accounted for by the absence of plasma. Inhibition of respiration in parasitized cells at very low concentrations of quinine was greater than occurs with normal cells. When the quinine concentration in the medium was greater than that obtained in the blood of chickens following effective therapeutic treatment of *P. gallinaceum* infections respiration and both the aerobic and anaerobic glycolysis of parasitized cells were inhibited to about the same extent. The effect on respiration was more marked with lactate or pyruvate as substrates. A useful comparative study showed that quinine also inhibited the formation of lactic acid from glycogen by muscle extracts in which the reactions involved are well known and the results should be of value regarding the mechanism of action of quinine. At concentrations of the drug within the range attained in effective therapeutic treatment in the same infection it was found that respiration was depressed, the glucose utilization was normal while there was increased formation of lactic acid. The degradation product of quinine obtained by KELSEY *et al* [this *Bulletin* 1944 v 41 923] was as effective as the parent substance in inhibiting *in vitro* respiration but affected aerobic and anaerobic glycolysis to a lesser degree.

J D Fulton

TALIAFERRO LUCY G COULSTON F & SILVERMAN M. The Antimalarial Activity of Tyrothricin against *Plasmodium gallinaceum*. *J Infect Dis* 1944 Nov-Dec. v 75 no 3 179-211 10 figs. [34 refs.]

The paper is notable as much for the wealth of observations recorded as for the results obtained in *P. gallinaceum* infection of chickens with a new type of antimalarial which is however very toxic. DUBOS (*Proc Soc Exp Biol & Med* 1939 v 40 311) described the bactericidal effect of an alcohol-soluble water insoluble extract of a soil bacillus on Gram positive cocci. From the crude product tyrothricin, crystalline neutral gramicidin and tyrocidine hydrochloride the crystalline salt of a weak base were later separated by HOTCHKISS & DUBOS (*J Biol Chem* 1940 v 136 803) [see also *Bulletin of Hygiene* 1939 v 14 886 1940 v 15 733 1941 v 16 650].

In the present experiments the crude product tyrothricin has been tested on *P. gallinaceum* infections of chickens and the results compared with those obtained with quinine. A few tests were also carried out with gramicidin. White Leghorn chicks were used ranging in age from 10 days to four weeks and were kept alternately in light and dark for periods of twelve hours at a time. The doses recorded below refer to the amounts administered per 100 gm. weight and during the experiment re-weighing was carried out every three days. A few infections were induced by the bites of infected *Aedes aegypti* mosquitoes and all others by inoculation of parasitized blood within half an hour of its withdrawal as parasites survived badly after that time. Daily blood smears were made at 9 a.m. to study the course of infection, and at 8 a.m. 2, 8 and 12 p.m. each day when the effect of the drug was being observed. The asexual cycle was followed by counting six classes of parasites ranging from the youngest forms to segmenters four times during the day as above. By counting all

parasites with two or more nuclei, which formed a fair percentage of the population a good indication of the periodicity was obtained. The percentage of degenerate forms of various classes of parasite was also estimated in studying the effect of each drug on the asexual cycle.

Tyrosin was prepared in 2 per cent. solution in 95 per cent. alcohol, and suitably diluted with distilled water before use. The drug was effective only when given intravenously, but oral and intraperitoneal administration was also tried. Quinine was given orally and intravenously as the dihydrochloride. In doses approaching the maximum tolerated, tyrosin caused respiratory failure in chickens, and was much more toxic than quinine. Doses of 0.2 mgm. per 100 gm. were tolerated intravenously daily for 15 days. Single doses of 0.6 mgm. were lethal. Its activity was compared with that of quinine when the latter was given orally and intravenously in sporozoite as well as in blood induced infections. The effect was additive when tyrosin was given intravenously along with quinine given orally in blood-induced infections. The inhibitory effect of both drugs on *P. gallinaceum* respiration *in vitro* was also measured.

It was found that continued treatment with 0.2 mgm. of tyrosin was as effective as with 16-24 mgm. of quinine orally in sporozoite-induced infections if treatment was started on the day of infection or on the first day of appearance of parasites. The parasite number was markedly reduced, but infection or relapses were not prevented, nor was the incubation period shortened. The drug was apparently not effective against sporozoites or cryptozoites, and, with a certain dosage, fatal relapses, accompanied by the presence of erythrocytic forms occurred. In blood-induced infections the same dosage of tyrosin was more effective and prolonged the incubation period. When larger doses of tyrosin were given over a shorter period, the results were not so satisfactory.

A study of the normal course of the asexual cycle in general, confirmed the results of earlier workers. The number of meronts per segment varied from 6 to 36. Atypical forms were present at the time of crisis. The effect of both drugs on the parasite and on the asexual cycle was observed when treatment was started at the early trophozoite stage. Tyrosin prolonged the cycle from the normal 36 to 48 hours and rendered it less synchronous. Twenty-four hours after the start of treatment degenerate multinucleate stages were noted. The larger trophozoites and fully developed asexuals were affected more than very young forms or gametocytes (cf. the results obtained by Hewitt & Richardson (this Bulletin 1944, 41: 183) in *P. lophurae* infections of chickens with other drugs, including quinine). The effects of this drug on different stages of the parasite are recorded in detail, and non-parasitized cells were also affected. Observations were made in the same way following quinine treatment. It appears that tyrosin does not affect reproduction of the parasites so markedly as quinine, its effect being predominantly inhibitory reproduction. Both drugs are, nevertheless, about equally active in controlling the infection. When the activity of the drugs given intravenously was compared in sporozoite- and blood-induced infections by starting treatment at different periods during the infection, it was found that 0.75 mgm quinine was equal to 0.2 mgm tyrosin (quinine equivalent approximately 4). On a weight basis tyrosin inhibited respiration of *P. gallinaceum* more effectively *in vitro* than did quinine and caused haemolysis of red cells, while the latter did not. The markedly curative and suppressive activity of tyrosin in this infection was paralleled by gramicidin, which, when given in doses of 0.4 mgm daily for 12 days, greatly reduced the number of parasites following blood-induced infections.

J. D. Fulton

BOSE A N & RAKSHIT P The Effect of certain Substituted Quinolone an
Acridine Compounds on the Gametocytes of *Haemoproteus columbae*
Quart J Pharm & Pharmacol 1944 Oct.-Dec v 17 No 4 319-22 1 fig
[12 refs]

An investigation of the activities of certain substituted quinoline and acridine compounds against the gametocytes of naturally acquired *Haemoproteus columbae* infections of pigeons has been carried out with the following compounds —

- I 6-methoxy-8-(γ -diethylaminopropyl) aminoquinoline in the form of its methylene-bis-salicylic acid salt.
- II 2-chloro-7 methoxy 5-(δ -diethylaminobutyl) aminoacridine in the form of its hydrochloride
- III 2 diethylsulphonamido 7-methoxy 5-(ω -diethylaminoisamyl) aminoacridine
- IV 2-diethylsulphonamido-7-methoxy 5-(δ -diethylaminobutyl) aminoacridine.
- V 4-aminobenzenesulphon-6 methoxy-8-quinolylamide.

Compound II had already proved very active in *P. knowlesi* infections of monkeys [this *Bulletin* 1944 v 41 828]. Six pigeons each weighing 300-350 gm. were treated with varying doses of each drug. They were kept in separate screened cages after being cleansed by pyrethrum soap. Five pigeons were used as controls. The blood of each bird was regularly examined and gametocytes counted for 7 days before treatment began. The number of infected red cells varied from 1 to 11 per cent. All drugs were given orally in glucose solution and in varied doses once each day for five consecutive days. The blood examinations were continued for four weeks or longer after the start of treatment. In the case of drug I doses ranged from 0.5 to 10 mgm. it was effective but relapses occurred. Drug II in doses of 1-10 mgm. also had some action in causing parasites to disappear. Drugs III and IV in 10 to 25 mgm. doses had only a slight action. Drug V in 10 to 25 mgm. doses had no effect on gametocytes. The authors consider that the method may have some useful applications [see COATNEY this *Bulletin* 1936 v 33 238]. In the case of effective drugs the results were clear-cut. Gametocidal effect is not permanent with any of them and is lowered when a sulphonamide group replaces chlorine in the acridine ring and also when the alkylamino side chain in the quinoline molecule is replaced by a sulphanilyl group.

J D Fulton

BLACKWATER FEVER.

SKIPPER E W & HAINE G L Blackwater Fever in West Africa. *Brit Med J* 1945 Mar 10 325-7 [19 refs]

Seven cases of blackwater fever occurring in the West African command are described. The authors give an account of the cases because it is felt that this disease is of special importance while British and Allied troops are living and fighting in countries in which it occurs and because it is not very rare for individuals to develop it after return to the United Kingdom from the Tropics. The descriptions of cases are disappointingly short and the tables would have been improved if they had contained more information especially regarding urine volume and urinary reaction. The relation of blackwater fever to malaria and anti malarial drugs is briefly discussed and FINDLAY (personal communication 1944) is quoted as stating

that "the incidence of blackwater fever in the West African Command has considerably diminished since the substitution of mepracrine for quinine as a suppressant and as the therapeutic drug for uncomplicated malaria.

The possible mechanisms of haemolysis in blackwater fever are discussed without reference to a good deal of the literature on the subject (for example, *POWDER, J. Gen. Phys.*, 1944 v 27 483 *OLIVER-GONZALEZ* [*this Bulletin* 1945 v 42, p. 353] *Fox and KORDI* [*ibid.*, 1945 v 40 883]).

The authors state in their summary that "evidence is produced to show that alkalis are probably of value in preventing anuria. This statement is no doubt based partly on the fact that all seven of the reported cases recovered and only one developed anuria. The authors make a plea for the early use of alkali, but are not very clear about the reason for its use beyond stating baldly that "in blackwater fever an acidosis is usually present, a statement which is not borne out by the very little work that has been done on this subject. The advice given concerning fluid intake includes no mention of limitation of intake in conditions of oliguria and anuria—a word of warning such as that recently expressed by *PARAMORE* (below) should have been added here, since it is so very easy to waterlog a patient who is not getting rid of fluid through his kidneys.

It is not clear from the text why the authors state that "blood [transfusion] should never be given if oliguria is present. Such advice is apparently based on the possibility of haemolysis of the donor's cells and indicates that the authors are concerned mainly with the possible effects of haemoglobin and its products on renal function, and not so much with the necessity of providing blood cells for the carriage of oxygen to vital tissues.

[There is a mistake in the second paragraph of the paper where it is stated that methaemoglobin is never excreted. It is presumed that the authors were referring to methaemalbumin, as they state in the preceding sentence that oxyhaemoglobin and methaemoglobin are excreted in the urine.]

B. G. Macgregor.

PARAMORE, R. H. Traumatic Anuria. [Correspondence.] Lancet 1945 Mar 10 323

Referring to the fatal case of traumatic anuria reported by *CAPLAN and DUCKERT* see [*Bulletin of Hygiene* 1945 v 42, 331] in which large quantities of fluid were given the author states that the condition of the kidneys found post mortem in that case is not unique but is common to all cases of anuria, even in soldiers wounded by high-explosive missiles as reported by *DARSHADY et al.* [*Bulletin of War Med.* 1945 v 5 487]. He warns against the pressing of fluids in cases of anuria and suggests that the time may come when clinicians will restrict the application of some of the methods—transfusion ice-packs to damaged limbs the horizontal position—which are in favour today. [The author expresses his inability to go deeply into the question in a letter and does not support his views on the treatment of shock and anuria with records of cases.]

J. F. CORSON.

TRYPANOSOMIASIS.

FAIRBAIRN, H. Sleeping Sickness in Tanganyika. Tanganyika Territory Medical Department Medical Pamphlet No 40 8 pp., 1 map. 1944 Dar-es-Salaam Govt. Printer

In this pamphlet the author gives a short account of the main features of Rhodesian sleeping sickness, with many practical hints on diagnosis, prognosis and treatment based on much experience in Tanganyika Territory.

He regards *Trypanosoma brucei* and *T. rhodesiense* as distinct species and holds the view that animals especially game are reservoirs of *T. rhodesiense* in nature as they have been shown capable of being in experimental work.

Diagnosis can always be made by blood examination and gland puncture is unnecessary but in some advanced cases it is more quickly made by lumbar puncture.

Prognosis [especially in natives who cannot give accurate histories] depends greatly on the protein content of the cerebrospinal fluid over a period of some months. A cell count of 7 per cmm should not be considered abnormal in cured early cases. The upper normal limit of protein [Sicard and Canteloube tube method?] is 0.025 per cent. If it is not above 0.03 per cent. the case is an early one of not more than six weeks duration and can be cured with suramin [germanin] alone. If the protein is between 0.03 and 0.035 per cent. a full course of trypanamide should follow the course of suramin while if the protein is 0.04 per cent. or more the case is a late one and most probably incurable.

There is little danger in making a lumbar puncture before treatment is given [this refers of course to the risk of pricking a vein while trypanosomes are present in the blood] the Howard Jones needle which has a small bore and is tough and made of stainless steel is recommended. The Sicard and Canteloube tube in which trichloroacetic acid is used to precipitate the protein is recommended for the estimation of protein in the cerebrospinal fluid.

Treatment—Injections of suramin should not be discontinued on account of the occurrence of albuminuria. It will not increase and will usually clear up within a month after the course of injections. At the end of the course of suramin a lumbar puncture should be made repeated a month later and afterwards at intervals judged to be necessary.

Vision should be tested (by picking a pin from the table) before each dose of trypanamide. If it is impaired trypanamide should not be given. Children bear trypanamide badly and the dose in grammes should be one twentieth of the age in years.

Repeated courses of trypanamide should not be given in relapsed cases besides the risk of producing optic atrophy there is the danger of making the trypanosomes arsenic fast. Relapsed cases should be treated by monthly injections of 1 gm. of suramin to sterilize the peripheral blood.

Prophylactic injections of suramin—The author believes that the risk of so-called cryptic infections is a real one and thinks it is preferable for an individual to get a definite attack that can be easily diagnosed and treated than a cryptic attack even if the chance of getting the latter may be smaller in the circumstances.

J. F. Cerson

NEGHEM A. Penicillin Sodium Treatment of Experimental Trypanosomiasis of Mice. *Science* 1945 Feb 2 115

The work was done on a few mice infected with *Trypanosoma cruzi* no beneficial effect was observed.

GASCHEN H. (Dr. des Sciences chef de travaux à l'Institut d'Hygiène Lausanne (Suisse)) Les Glossines de l'Afrique Occidentale Française (The Tsetse Flies of French West Africa.) *Acta Tropica* Basel 1945 Suppl. 2, 131 pp., 114 figs & 1 folding pl. [Bibliography]

This book is reviewed on p. 512.

[June 1945]

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UNES, Vladimir [D.M.V., Director del Instituto de Investigaciones Veterinarias]
 El *Trypanosoma* *char* Americano agente de la Tripanosomiasis Bovina en
 Venezuela, en Comparación con el del África. [American T. v. *char* the Causative
 Agent of Bovine Trypanosomiasis in Venezuela Comparison with that in
 Africa.] *La Conferencia Interamericana de Agricultura, Caracas, No 1 Caracas.*
 1944 pp xi+124 20 figs 10 tables & charts [85 refs.] [In Spanish English
 summary pp. 111-117]

This book was reviewed on p. 422.

LEISHMANIASIS.

ROSE H. M. Cold Hemagglutinins in Visceral Leishmaniasis (Kala-Azar) Proc
 Soc. Exper Biol & Med 1945 Jan. v 58, No 1 83-4

Cold agglutinins in high titers were demonstrated in the blood of two
 patients suffering from visceral leishmaniasis. In one of these patients who was
 followed for several months, the agglutinins returned to within normal limits
 after recovery

BAKHRAMI D. A. [Culture of *Leishmania tropica* in Chick Embryo] Doklady
 Akademii Nauk U.S.S.R [=C.R. Acad. Sci. USSR.] Moscow 1943 NS
 v 40 No. 5 238. [In Russian.]

The author describes a method for cultivating *Leishmania tropica* in the chick
 embryo. The eggs are first incubated for six days at 39°C. after which two
 holes are bored in the egg, one leading to the air-sac, and the other to the
 embryo. After the leishmania (cultural forms or L.D. bodies from sores) are
 introduced through the second hole, both openings are sealed with paraffin wax,
 and the eggs are incubated at 25°C. Three days later leishmania can be found in
 large numbers in the chorioallantois and in the embryo itself, in which they
 assume the leptomastigote stage and in the embryo itself, in which they
 in cultures on artificial media. C. A. Hoare.

KOJEVNIKOVA, E. V. [Localization of Cutaneous Leishmaniasis according to
 its Type.] Med. Parazit. & Parasitic Dis. Moscow 1944 v 13 No. 2,
 88-9 [In Russian.]

As is known, the lesions of cutaneous leishmaniasis are usually formed on the
 exposed parts of the body. Though their localization may vary in the published
 accounts of some observers the site most commonly affected is said to be the
 face while in those of others it is the limbs. A comparison of the literary data
 has convinced the author that the former were dealing with cases of the dry
 late ulcerating type, while the latter were dealing with cases of the moist
 early ulcerating type (see this Bulletin 1944 v 41 331). The author herself
 examined from this point of view 3 125 case histories of oriental sore of which
 1 620 were of the dry type and 1,505 of the moist type. This study fully
 confirmed the conclusions based on the works of previous authors, for it was
 found that in the moist type the great majority of lesions were restricted
 to the extremities whereas in the dry type the face was mainly affected.
 C. A. Hoare

KLITZNER H Ueber die therapeutische Beeinflussbarkeit der Hautleishmaniosen durch Sulfonamide. [The Treatment of Oriental Sore with Sulphonamide.] *Deut. Militärarz* 1943 Aug v 8 No 8 472-4 4 figs.

Having in his care three cases of oriental sore in soldiers who had served in N Africa, the author treated them by administering Albucid [sulphacetamide] by the mouth and applying to the sores an ointment containing the same drug. Healing of the sores took place in periods up to 48 days. Though he recognizes that a sulphonamide may aid the healing of oriental sore by getting rid of secondary bacterial infections, he still thinks that the drug may have some specific action. He does not say how long the sores had been in existence when treatment was initiated nor whether spontaneous healing had already commenced.

C M Wenyon

FEVERS OF THE TYPHUS GROUP

ELFORD W J & VAN DEN ENDE M. Studies on the Viability and Filterability of Typhus Rickettsiae. *Brit J Exper Path* 1944 Dec. v 25 No 6 213-20

This paper deals with the results of investigations undertaken as an essential preliminary to a more comprehensive programme of typhus research. It must be read in the original form by workers engaged on similar enquiries, but some of the findings of general interest are as follows.

Suspensions of murine rickettsiae were found to retain their viability for a longer time when diluted with serum broth than when other media were employed. The paper by ANDERSON [this *Bulletin* 1945 v 42 106] who found skim milk the best of the media tested by him, came to hand after this paper had been sent for publication.

Suspensions in serum broth best retained their viability when the pH of the medium was between 6 and 8.5.

At -77°C . the viability of suspensions in serum broth pH 7.6 remained unimpaired for many days. At higher temperatures from -10°C . and upwards it was soon lost.

By filtration tests through membranes of the gradocol series it was found that suspensions of murine and two epidemic strains passed through membrane 700 millimicron but not through one of 500 millimicron pore size. Even with the 2,300 millimicron clearing membrane there was a reduction in the titre of infectivity and this reduction progressively increased with the use of smaller pore membranes and was considerable when membrane 700 millimicron was used. The authors consider that the smallest phase of the pleomorphic rickettsiae was unlikely to be less than 0.4 to 0.5 μ in diameter or width.

Estimations of the size of the organisms based on photographs of moist preparations of rickettsiae taken by ultraviolet light were made. The width was relatively uniformly 0.45 μ and the length varied from 0.6 to 1.8 μ . Photographs taken with the electron microscope gave similar results when allowance was made for shrinkage due to drying of the film. This was found to be 25-33 per cent.

John W D Megaw

OSBURN L W Alum-precipitated Typhus Vaccine. South African Epidemic Typhus Vaccine prepared from Gerbils (Genus *Tatera*). *South Africa J Med Sci* 1944 Nov v 9 No. 4 143-9 [13 refs.]

Gerbils (*Tatera afra* and *T. brandi*) were exposed to an X ray dose of 600 R. and afterwards inoculated intraperitoneally with 1.0 cc. of a yolk sac suspension

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of *Rickettsia prowazekii* estimated to contain about two billion organisms per cc. [presumably 2,000,000,000,000].
The animals became moribund within 48 to 72 hours and were then killed.
[This rapid effect suggests the action of a very large dose of exotoxin.]

Peritoneal washings, after treatment described in the paper were precipitated with alum and a vaccine was prepared. After preliminary tests on guinea pigs the dose selected for experiments in protection was 1.0 cc. estimated to contain one billion rickettsiae.

On a basis of a series of comparative tests, the author concluded that the alum-precipitated vaccine conferred better immunity than the non-precipitated vaccine of the same strength against South African and European strains of typhus rickettsiae. The results of the various tests, taken together and expressed in percentages would bear out this claim. The precipitated vaccine conferred complete immunity on 68 per cent. of guinea pigs and the non-precipitated protected only 37 per cent. when given in a single dose in three sets of tests.

But the results in different lots of guinea pigs appear to have been very variable. From the figures given in the tables the reviewer has extracted the following —

	Protection (one dose precipitated vaccine)			Protection (three doses ordinary vaccine)		
	Complete	Partial	None	Complete	Partial	None
	8 8 20	2 0 0	5 0 0	4 10 40	0 0 8	8 0 9

Table II
Table III
Table IV

Similar variations occurred in the results of the tests with single doses of non-precipitated vaccine of one lot of 15 guinea pigs, no less than 11 remained completely unprotected yet in three other lots totalling 20 animals all were completely protected.

The figures given in Table IV of the paper show the results of tests of protection against four European strains of epidemic typhus. In the case of each strain three lots of guinea pigs were vaccinated with one, two and three doses respectively of non-precipitated vaccine with the anomalous result that a single dose gave complete protection to 16 out of 19 animals, two doses gave similar protection to 15 out of 19 and three doses to 40 out of 57. In the other series of experiments three doses of this vaccine gave complete protection to 70 per cent. of the animals tested, whereas one dose gave similar protection to only 37 per cent.

Although these unexplained variations must be taken into account in assessing the significance of the findings it is evident that with the vaccines used by the author the balance of advantage rested with the alum-precipitated preparations.

John W. D. McGraw

FAIRSTEIN S. G. [Efficacy of Anti-Typhus Vaccination in Moscow Railway Workers.] *Gigiena i Sanitariya*. Moscow 1944 No. 10-11 34-9 [In Russian.]

A formalinized suspension of lungs of mice with rickettsial pneumonia was used as vaccine. Each member of the personnel of all railway stations in Moscow was given three injections of 0.5-1 cc. at intervals of 5 to 10 days. In all 8,316 people were vaccinated while 4,484 served as unvaccinated controls.

All subjects were observed for nine months. Reactions occurred in a small proportion of cases (local 5 per cent. general 9 per cent. rise of temperature 5 per cent.)

Seven cases of typhus occurred in the vaccinated group during the period of observation (=11 per 10 000). Two were mild occurring one month after the last injection 4 moderate occurring up to 4½ months and one fatal after 4½ months.

In the control group 18 cases occurred (40 per 10 000) one mild six moderate and 11 severe of which two were fatal.

D J Bauer

CASANEDA M RUIZ & SILVA R. Simultaneous Infection of Laboratory Animals with Murine and Classic Typhus. Immunological Results. *Proc. Soc. Exper Biol. & Med.* 1944 Oct. v 57 No 1 80-82.

The authors found that mice inoculated intranasally with mixtures of murine and classical rickettsiae died, within 48 hours of generalized pneumonia. Intranasal transfers from mouse to mouse were made for 13 passages and then failed because of secondary infection. There was evidence which will be presented in a later paper that both types of rickettsiae persisted for 10 passages.

Rats infected in the same way died of pneumonia in 72-96 hours but transfers failed after two passages because of secondary infection. From the lungs of rats infected in this way saline suspensions were prepared and were injected into guineapigs by the intradermal route. The sera of the guineapigs were subjected, 20 days later to complement-fixation tests in which classic murine and bivalent rickettsiae, respectively were used as antigens a response of 4+ at a titre of 1-80 was obtained with all three antigens the response at a titre of 1-160 was 2+ with classic antigen 3+ with murine and 1+ with the bivalent antigen. From these tests combined with comparative tests on the sera of guineapigs inoculated intradermally with monovalent murine and classic rickettsiae the authors conclude that the bivalent antigen acts as a mixture of murine and classic rickettsiae.

Vaccine prepared from the lungs of rats infected intranasally with mixtures of murine and classic rickettsiae gave a better degree of protection to guineapigs inoculated with classic rickettsiae than vaccines prepared from murine rickettsiae alone the authors conclude that classic rickettsiae multiply more readily in rats when the inoculum contains murine rickettsiae in addition.

The experiments are regarded as furnishing evidence of the superiority of bivalent rat lung vaccines over rat-lung vaccines prepared from murine strains only

John W D Megaw

TOPPING N H. & SHEAR M J. Studies of Antigens in Infected Yolk Sacs. *Pub Health Rep Wash.* 1944 Dec. 29 v 59 No 52 1674-5

Suspensions of epidemic typhus rickettsiae grown in yolk sacs were treated with ether and centrifuged. The resultant supernatant fluid was found to contain a substance, provisionally described as soluble which had the same immunological properties as the rickettsial sediment.

The material used for testing the supernatant fluid was prepared by certain modifications of an ether treatment method already employed by CRAIGIE who described his technique to the authors in a personal communication.

The authors method was to grind infected yolk sacs with alundum, dilute them with saline containing 0.5 per cent. formalin to make a 10 per cent. suspension, add an equal volume of ether shake and allow to stand for 1-1½ hours then apply repeated extraction of the aqueous phase (either once or twice) until the excess ether is colourless. The ether was removed at room

temperature under reduced pressure. The suspension was centrifuged at 4 000 r.p.m. for an hour and the sediment was resuspended in saline to the original volume.

The supernatant fluid and the rickettsial suspension were separately tested for their power to fix complement in the presence of immune guinea pig serum. In each of the two comparative tests given as examples the complement fixation titre of the supernatant fluid was greater than that of the rickettsial suspension the respective titres in one test were 1-128 and 1-64 in the other they were 1-64 and 1-32.

The supernatant fluid, after centrifugation at 15 000 r.p.m. lost little of its complement-fixation power and the sediment resulting from this process contained no complement fixing antigen.

The sample of supernatant fluid which originally had a complement-fixing titre of 1-64 was passed through a Berkefeld N filter and was then found to have a titre of 1-16.

Supernatant fluid injected intravenously into rabbits caused a rise in the Weitz-Felix titre from practically negative to 1-320. The rickettsial suspension caused a similar rise.

Guinea pigs inoculated with supernatant fluid developed immunity against typhus rickettsiae to at least the same degree as those inoculated with rickettsial suspensions. Their sera also developed complement-fixing antibodies to a rather higher average titre than the sera of guinea pigs inoculated with rickettsial suspensions.

Although the authors refer to the hummising antigens contained in the supernatant fluid as soluble they do not exclude the possibility that some of them may be contained in very small rickettsiae. [See also GROSS, this Bulletin 1945 v 42, 368.]

John W D McGraw

DURÁN C. M. Histopatología de las lesiones del tifo exantemático—primera investigación hecha en Guatemala. [The Histopathology of the Lesions of Exanthematic Typhus Fever.] Bol. Oficina Sanitaria Panamericana 1944, Sept., v 23, No. 8 791-5 8 figs. English summary.

This paper contains an illustrated description of the specific typhus nodules known as Friesel's nodules. These are liable to be confused with the myocardial lesions called Aschoff's nodules, which are however quite distinct being of anaphylactic origin and resulting in cicatrix formation. The latter contain numerous fibroblasts and eosinophiles which are absent from the typhus nodules.

The fundamental lesion of typhus is regarded as being an endothelial necrosis of varying intensity. There may be desquamation of the cells or thromboarteriolitis.

The most interesting feature of the study was that in some cases testicular lesions were found, consisting of capillary endothelitis and congestion of the parenchymatous tissues. These lesions have been regarded by some workers as occurring only in Rocky Mountain spotted fever and never in louse-borne typhus. [See also McGraw, this Bulletin 1945 v 42, 368.]

John W D McGraw

RANDERATH, E. Pathologisch-anatomische Erfahrungen bei Fleckfiebernekthosen. [Findings in the Pathological Anatomy of Typhus Fever.] Dtsch. Mikroskopist 1943 July v 8, No 7 376-80 1 fig (13 refs.)

A summary is given of the autopsy findings among the civil population of an occupied Soviet territory during a period of 18 months. The exanthem could be detected by microscopical methods up to as late as the 37th day in some cases. In others there was no trace of its presence on the

23rd day Typhus nodules had disappeared by the 31st day they were never found in the heart, which showed a condition of typhus myocarditis with oedema of the interstitial tissues and infiltration of these by macrophage cells together with a very few plasma cells and lymphocytes.

Among the lesions due to complications the most striking was a diffuse haemorrhagic glomerulonephritis during the winter months this occurred in about one-quarter of the cases Bowman's capsules and the lumen of the renal tubules were sometimes packed with red cells. Haemorrhages into the other organs were not seen and even the rash was seldom petechial.

Icterus was not infrequent it was associated with a serous hepatitis and was most common in persons who had died during the first or second week. There was a suspicion that it might have been due to epidemic hepatitis lighted up by the typhus infection.

Diphtheria sometimes accompanied by a haemorrhagic bronchopneumonia was a surprisingly frequent complication which often had not been diagnosed during life.

Suppurative parotitis was the chief septic complication Gangrene of the extremities was quite uncommon.

Circulatory failure was believed to be due to damage to the vasomotor centres and to be associated with the condition of the peripheral vessels rather than with myocarditis.

John W D Megaw

- v STOCKERT Die neuropathologischen Syndrome des Fleckfiebers. [The Neuro-Pathological Syndromes in Typhus Fever] *Deut. Mikrobiol.* 1943 June v 8 No 6 327-30

The author discusses the association existing between the numerous nervous manifestations of typhus fever and the localization of the lesions in different parts of the central nervous system

He describes three chief syndromes —(1) The mad brain syndrome with disturbances of consciousness somnolence, delirium and disorders connected with the vegetative nerve centres. The most important of the last named disorders is the characteristic fall of blood pressure but how far this is due to loss of tone of the peripheral vessels and how far to myocarditis is still a matter of conjecture there is however evidence of disturbance of function of the vegetative nerve centres. (2) The bulbar symptom-complex in which there are auditory disturbances and signs of parasympathetic irritation. (3) The extra pyramidal syndrome with choreiform movements or rigidity

John W D Megaw

- Rykov N V [An Improvement of Minkievich's Modification of the Weil-Felix Reaction.] *Zhurnal Mikrobiologii Epidemiologii i Immunobiologii*, Moscow 1944 Nos. 1-2 42. [In Russian.]

The following is a translation of this short paper —

Having carefully verified Minkievich's reaction with haemolysed blood on a slide and compared it with the classical Weil-Felix reaction the author introduced a quantitative method of estimation as the result of which a complete parallelism of both reactions was observed, especially in the mutual dilutions. A coincidence of the results was noted in 97 per cent. of the reactions. Furthermore in order to avoid the necessity of using a hand lens in examining the finely flocculated suspension after agglutination at the usual concentration (3 milliard per 1 cc.) the author increased its density to 15 milliard per 1 cc. by centrifuging 10 cc. of the suspension at 4 000 revolutions for half an hour the fluid is then

temperature under reduced pressure. The suspension was centrifuged at 4,000 r.p.m. for an hour and the sediment was resuspended in saline to the original volume.

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A summary is given of the autopsy findings among the civil population of an occupied Soviet territory during a period of 16 months.

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decanted, and to the sediment are added 2 cc. of physiological saline solution. This concentrated suspension, when used in drops together with haemolysed blood, produces a distinct agglutination in from $\frac{1}{4}$ to 3 minutes in dilutions up to 1:64."

C. A. Hoare

TOKAREVICH K. V. [Laboratory Infections with Typhus Fever as Material for Discussion of the Problem of the Mechanism of Infection.] *Zhurnal Mikrobiologii, Epidemiologii i Immunologii* Moscow 1944 Nos. 1-2, 28-9 [In Russian.]

A description is given of five cases of accidental infection of the laboratory staff with typhus fever. In two of these transmission was by the droplet method, in two others by dry faecal particles of the lice being deposited on the mucous membrane, and in one by accidental injection with a pipette of teased-up louse-intestines. The course of the disease was severe or of medium severity in three unvaccinated patients while in the two who had previously been vaccinated it ran a mild course. From these cases it is seen that in spite of the different methods of dissemination and portals of entry the rickettsiae provoked in all of them the typical disease though considerably milder in the vaccinated persons.

The successful infection of vaccinated persons described in this paper is in contradiction with the consistently negative results obtained previously when feeding infected lice on vaccinated persons (2,000 observations). The author suggests that this discrepancy is due to the fact that in the laboratory infections the rickettsiae were mature and were introduced in massive doses whereas the vaccinated persons on whom infected lice fed, received only small doses of rickettsiae from recently infected insects. It is concluded from these observations that immunization with killed rickettsiae does not afford complete protection against infection with typhus fever.

C. A. Hoare

GRONASHEVSKY L. V., BAGROVA, A. S. & STEPANOV I. R. [The Nature of Interruptions in the Course of the Incidence of Typhus Fever in the Affected Populated Localities.] *Zhurnal Mikrobiologii, Epidemiologii i Immunologii* Moscow 1944 Nos. 1-2, 17-28 [In Russian.]

17

In a previous communication the authors have demonstrated that the occurrence of new foci of typhus fever is always due to the introduction of the infection from some other focus but not to the preservation of the rickettsiae in healthy human carriers or elsewhere. In the present paper the authors deal with the epidemiology of inhabited localities, representing foci of typhus fever in which there is an irregular alternation of months in which there occur cases of the disease and months in which no cases are recorded. From observations, carried out in 367 places of this type and subjected to a detailed statistical analysis, the authors arrive at the following conclusions —

- (1) The more a given territory is affected, the more frequently there are found in it inhabited places, which do not exceed 1-2 months, are often misleading for in such cases the continuity of the epidemic is actually maintained by unreported cases who are kept in their homes. (2) When there is a genuine interruption in the incidence, lasting over two months, the infection of the disease can only occur as the result of a new introduction of the infection from some other focus. (3) The complete eradication of typhus fever throughout the country can only be effected by rapid liquidation of every newly-established focus of the disease followed by close observation in the course of two months. (4) The detailed study of the epidemiology of typhus fever fully supports the

view that patients suffering from the clinical form of the disease as well as lice who have fed on them represent the only sources of infection. [See also this Bulletin 1942 v 39 141] C A Hoare

SHUBLADZE A. K. SOLITERMAN P. L. & STERNGOLD E. J. [Sera against typhus Typhus Fever] *Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii* Moscow 1944 Nos 1-2 35-7 [In Russian.]

After describing previous attempts to obtain a specific serum against typhus fever the authors give an account of their own results with a serum prepared with an antigen obtained from the lungs of mice infected intranasally (two inoculations) with the blood of patients and brain emulsion of experimentally infected guinea-pigs. This strain of rickettsia was passaged into another series of mice the lungs of which were teased up in saline with the addition of 0.2 per cent formalin and used for the immunization of four horses. These were immunized in various ways with different doses intravenously and subcutaneously. The sera obtained from the horses gave a positive Weil Felix reaction with *Proteus X19* in dilutions from 1:640 upwards as well as a positive Weigl reaction (rickettsia agglutination) in a dilution of 1:320. The neutralizing prophylactic and therapeutic effect of these sera was tested on guinea-pigs. It was shown that they were capable of neutralizing 100 infective doses of rickettsiae (Otto strain) when introduced subcutaneously into these animals on the first day after infection they arrested the development of the disease while on the fifth day they sometimes improved and shortened the course of the disease. The results of preliminary clinical tests of these sera appeared to be promising. C A Hoare

Kovács G & v KUP J. Neue Beiträge zum Krankheitsbild und zur Behandlung des Fleckfiebers [A New Contribution on the Clinical Aspects and Treatment of Typhus Fever] *Wien Klin Woch* 1944 June 2 v 57 No 21/22 234-8 4 figs.

The authors treated a large number of cases of typhus fever during the early months of the present year [presumably 1944]. The incubation period ranged from 5 to 21 days. In a few cases the onset was sudden with rigor but usually the temperature rose steadily during the first two or three days during which there was headache with pains in the lumbar region and joints.

In about 50 per cent of the cases the fever was of the continued type in the other cases daily remissions of 1-1.5°C occurred. There was leucopenia during the first 5-8 days then leucocytosis gradually developed. In mild attacks the rash was inconspicuous sometimes even absent. In severe cases the usual type of rash was morbilliform occasionally it was scarlatiniform. It was haemorrhagic in 6 per cent of the patients. The palms and soles were the only parts of the body that were uniformly exempt from rash. Gangrene and bedsores were quite exceptional. Pneumonia occurred in only two cases and in them its onset was 14 days after desquescence.

Traces of albumin were found in the urine of 10 per cent of the patients no casts or blood cells were found except in one case in which there was haematuria lasting two days. Nervous symptoms were few only one patient attacked his neighbour in the next bed.

Prolonged coagulation time low blood pressure and a condition of collapse were attributed by the authors to failure of the secretion of the adrenals which was regarded as the usual cause of death in uncomplicated cases. Myocarditis was believed to be of secondary importance.

Mention is made of the use of a specially sensitive strain of *Proteus* X19 by which a significant agglutination reaction could be obtained within the first few days—sometimes even within 36 hours.

The authors claim that their system of treatment was responsible for the mildness of the nervous symptoms and the rarity of complications but in the absence of comparable controls or other reliable evidence an attitude of caution seems to be justified.

Ultraseptyl" (sulphamethylinthazol) in doses of 5 cc. together with 10 cc. of 20 per cent. dextrose solution, was given once daily intravenously for five days in average cases and for seven days in severe attacks. This was followed by daily intravenous injections of 10 cc. of 20 per cent. sodium chloride solution for 8-10 days "also with dextrose [presumably together with 10 cc. doses of 20 per cent. dextrose]

The salines were given to stimulate the activity of the adrenal glands

John W. D. Megaw

v BORMANN F. Erfahrungen neber Fehris neuralgia periodica (Fünftagefieber) bei einem Truppenteil. Observations on Neuralgia-Periodic Fever (Trench Fever).] *Deut. Militärarz* 1943 Aug., v 6, No 8 457-63 3 charts

This paper deals with an outbreak of trench fever already described by the author [see this *Bulletin* 1943 v 40 838]

Points brought out more clearly here are (1) that abortive attacks lasting one to three days are far more frequent than is generally supposed—about 40 per cent. of the cases seen by the author were of this type and he states that they rarely find their way to the hospitals (2) that shin-bone pains occurred in less than half of the cases and had little diagnostic value because they occurred also in typhoid fever typhus fever influenza, and Weil's disease and (3) less than one-third of the attacks were of the periodic type and in these the periodicity was highly irregular

John W. D. Megaw

IRONS, J. A., BOSHS, S. W. THURMAN, D. C., Jr & MCGREGOR, T. Probable Role of the Cat Flea, *Ctenocephalides felis* in Transmission of Murine Typhus. *Amer. J. Trop. Med.* 1944 Nov. v 24 No 6, 359-62.

Between November 1st and 10th 1942, all three members of a family in Austin Texas, fell ill with typhus fever and it was suspected that the infection had been acquired from a flea infested kitten brought from a local "feed store" about ten days before the onset of the first illness.

The kitten had been destroyed, but two others of the same litter were obtained and from them about 200 fleas identified as *Ctenocephalides felis* were collected. From two of three pools of fleas each containing about 55 specimens murine rickettsiae were isolated by intraperitoneal inoculation of guinea-pigs. Suspensions of the eggs of the fleas inoculated in the same way gave negative results.

Another person was found to have become infected with typhus a few days after having obtained two kittens from the same store and some of the employees of the store were said to have had illnesses suggestive of typhus during recent years. The store was rat-infested, and a strain of murine typhus was isolated from a rat caught near the store.

The strength of the solution (presumably of the sodium salt) is not stated the drug has been given by mouth in doses similar to those of other sulphonamides, but it has caused severe neuritis in some cases [see *Bulletin f Hygiene* 1941 16 269 and *Bulletin f War Medicine* 1942, v 3 44. For other references see *Bulletin f Hygiene* 1940, v 15 635 1941 v 17 537 1942, v 18 840 and *Bulletin f War Medicine* 1940 v 1 116 1942, v 2, 236 1942, v 3 227—Ed.]

About December 2nd 1942 one of the laboratory technicians who had been engaged 10-12 days previously on work with the infected fleas fell ill with a fever which lasted nine days the Weil Felix reaction was negative on the 6th day and became positive 1-320 on the 12th day. Suspensions of the brains and spleens of the kittens from which the fleas had been collected were injected intraperitoneally into guineapigs with negative results.

In May 1943 a cat and her kittens from the store were investigated no infection could be detected in their fleas and the kittens were found to be unsuceptible to inoculation by murine rickettsiae. Brains and spleens of these kittens taken on the 14th day after inoculation failed to infect guineapigs.

The authors are inclined to the view that the cat fleas had acquired the infecting agent from the kittens they mention the possibility that the fleas might have bitten an infected rat but they think this unlikely because they had never found cat fleas on rats and they state that PRICE [this *Bulletin* 1943 v 40 775] found only three cat fleas in an examination of 4 188 rats in the western United States. They point out that their exceptional finding does not in any way invalidate the fundamental importance of the rat and its fleas in the epidemiology of murine typhus.

Hardly any other cases of typhus were seen by physicians in Austin Texas during the year 1942. [It is to be hoped that the cat will not be proved to be a reservoir of infection. In any case its activity in controlling the rat population is likely to do more than compensate for rare incidents of this kind.]

VAN ROOYEN C. E. & DANSEIN D. Transmission of Imphal Scrub Typhus Infection to Egyptian Desert Rodents. *J Path & Bact* 1944 Oct v 56 No 4, 570-72. John H. D. Megaw

In December 1943 Captain PARRY R.A.M.C. inoculated guineapigs with blood from scrub typhus patients at Imphal on the Assam Burma border. From the guineapigs Major M. T. PARKER transmitted the disease to white mice which provided the infected material used in the present experiments. The dates of the transfers are not mentioned.

Mouse brain suspensions from the infected mice were injected intra peritoneally into two species of Egyptian gerbills *Gerbillus gerbillus* and *G. pyramidum* also into a jerboa *Jaculus jaculus*. All these animals proved to be highly susceptible. After an incubation period of 12-14 days they became ill and eventually most of them died. The febrile reactions are not mentioned. When passages were made with brain substance the incubation period after 12 transfers was 10-12 days when peritoneal exudate was used, it was 7-10 days. The fatality rate in *G. gerbillus* was 100 per cent in *G. pyramidum* it was 65 per cent.

Enlargement of the liver and spleen with exudate into the peritoneal and pleural cavities were the most conspicuous features at autopsy.

Smears of the exudate after the 12th passage were stained by a modified Giemsa technique and also by Jenner's stain followed by Giemsa. Cells in the exudate contained rickettsiae and large numbers of the organisms were found outside the cells. The appearance is said to have been exactly similar to that illustrated in the report by LEWTHWAITE and SAVOOR [this *Bulletin* 1936 v 33 424 921 and 922 *ibid* 1937 v 34 473 and 474] on scrub typhus in Malaya.

The rickettsiae could not be demonstrated by Macchiavello's method of staining. In the jerboa the effects of inoculation were very similar but the peritoneal exudate was more abundant. Death usually occurred two days after the onset of the illness.

John H. D. Megaw

SHKORBATOV V. L. [On the Results of Work by the Epidemiological Section of DVIEM on Tick-borne Typhus Fever in Khabarovsk Province.] *Zhurnal Mikrobiologii Epidemiologii i Immunobiologii* Moscow 1944 Nos. 1-2, 43-6 [In Russian.]

The author records miscellaneous epidemiological observations and experiments on tick borne typhus fever carried out by the Far Eastern Institute of Experimental Medicine (DVIEM) in the Khabarovsk province. It was found that the rickettsiae could be readily isolated both from the blood of patients during the pyrexial period and from ticks (*Dermacentor sylvarum*) at different periods of their development by intraperitoneal inoculation of vitamin-deficient guinea-pigs. Hereditary (transovarial) transmission of the infection followed up to the second generation proved to be the rule in ticks. The skin reaction ("primary effect") similar to that in man was obtained in guinea-pigs subjected to bites of both infected and non infected ticks but not in rabbits. In man there does not appear to be any definite correlation between the skin reaction at the site of tick bites and the development of an infection but as a rule, a reaction is present in positive cases. The blood of persons suffering or recently recovered from tick borne typhus fever reveals the presence of agglutinins for *Proteus OX19* OX2 and OXK the first named usually being in highest titre and most persistent. The simultaneous production of agglutinins for three or two of these organisms is rarely observed. The usual titre for *Proteus OX19* is from 1:400 to 1:800 whereas the maximum titre for OX2 and OXK does not exceed 1:200.

Considering the high degree of exposure (=70 per cent) of the population of the endemic focus to bites by ticks, the incidence of typhus fever (up to 3 per cent.) among those bitten is insignificant. It would, therefore appear that either the infection rate among the ticks under natural conditions is low or that the susceptibility of human beings to this infection is low. In any case it would seem that the degree of infection in ticks does not play an important rôle in the epidemiology of the disease in question.

C. A. Hoar.

EDMONDS P. K. Rocky Mountain Spotted Fever Treatment with Penicillin. *Rocky Mountain Med J* Denver 1944 Dec. v 41 910 [Summary taken from *J Amer Med Ass* 1945 Feb 24 v 127 No 8 490]

Edmonds reports that a boy aged 14 who became ill with high fever, chills, headache, backache, vomiting and general malaise was admitted to the hospital and was given sulfonamides as a matter of routine. These proved ineffective. A diagnosis of Rocky Mountain spotted fever was made and was corroborated by a history of tick bites and an increased agglutination dilution for Rocky Mountain spotted fever. One hundred thousand units of penicillin was added to 500 cc. of isotonic solution of sodium chloride and given by drip intravenously. Within two hours the temperature which had been between 104 and 105 F. dropped to 100 F. and there was a definite improvement in the patient's condition. The boy recovered. The author hesitates to draw conclusions from one case, but he hopes that penicillin will be tried by others in Rocky Mountain spotted fever so that its benefits will be either proved or disproved.

YELLOW FEVER.

JACOBS H R. Prolonged Viability of Yellow Fever Virus in Serum Mixtures containing Ammonium Sulfate. *Proc Soc Exper Biol & Med* 1944 Nov 1 57 No 2 260-61 1 fig

Simple saline solutions are rapidly lethal to yellow fever virus and although serum protein has a strongly preservative action serum and saline mixtures are at best not very effective. Since intracellular media are slightly acid the author tried the addition to media of salts that would give it a slightly acid reaction and in this paper he gives the results of a trial of ammonium sulphate. Ammonium sulphate was added in 3 per cent. and 1 per cent. amounts to a mixture of human serum sodium chloride and yellow fever virus this formed commonly used in routine experiments with yellow fever virus. The control mixture and contained 10 per cent. of normal human serum 0.4 per cent. of sodium chloride and 10 per cent. of a 10^{-2} suspension of yellow fever virus. The three mixtures were incubated continuously at 37°C . and were tested daily by injecting 0.03 cc. into standard white mice the viability of the virus being measured by its capacity to cause illness and death in mice between the 4th and 10th days.

The 1 per cent. ammonium sulphate mixture appeared to have the optimum strength as was confirmed by further experiments much living virus was retained for 6 days and an appreciable amount to the 8th day. At $22-25^{\circ}\text{C}$. and shielded from light full strength of virus was preserved for 20 days. The pH of the medium was the important factor the optimum being 6.3-6.5 and this was produced by the addition of 1 per cent of ammonium sulphate. J F Corson

HECHT O & ARDUZE P J. Contribución al conocimiento de la fauna Calicidiana de la parte norte de la Guayana Venezolana. [Coleleidae of Bolívar State, Venezuela.] Reprinted from *Bol Entom Venezolana* 1944 Sept 30 v 3 No 3 105-18. [16 refs.] English summary

This study was undertaken in Upata a district near Ciudad Bolívar in Venezuela in order that light might be thrown on the presence of jungle yellow fever in those parts. In all, three survey expeditions were made the first in April-June 1943 the end of the dry season and the start of the rains the second in September-December 1943 at the end of the rains but when heavy showers are frequent the third a short visit of 11 days towards the end of June 1944. Large numbers of larvae were seen in the pools in the first visit also in holes of trees and in casumbas recently filled with water [Casumbas are hollows in the rocks which may retain flood water for long periods] In the latter part of this visit *Haemagogus* (three species) and *Sabethes* sylvatic mosquitoes were found more of these were caught in the second expedition and still more in the third. In the same situations were found *Wyeomyia* and such sylvatic mosquitoes as *Finlaya* and *Compostegus* together with *Aedes*. Two species were found which are believed to be new records for Venezuela namely *Aedes* (*Compostegus*) *leucocelaenus* and *Culex* *brevispinosus* there is also *Aedes* (*Finlaya*) *upatensis* which had previously been reported by ARDUZE and HECHT. A few notes are given as to the habitat of 43 species and a table showing the species distribution and habitat of 12 in which the yellow fever virus can persist of seven which can transmit the virus by their bite and three which have been found naturally infected namely *Aedes leucocelaenus* *Haemagogus capricornis* and *Sabethes*. [A useful pamphlet for reference.]

H Harold Scott

PLAGUE.

SAVINO E. & GOOBAR J. K. La peste rural en el departamento de Rio Seco (Córdoba). Su estudio epidemiológico con especial referencia al *Graomys griseoflavus centralis* como depósito de virus pestoso así como también el hallazgo de peste espontánea en algunos roedores agrestes y en gatos domésticos. [Rural Plague in Rio Seco (Córdoba) Argentina.] *Rev Inst Bacteriológ* Dr Carlos G Malbran Buenos Aires. 1944 Sept., v 12, No 3 287-92. [14 refs.]

Some of the figures relating to this survey have already been given (this Bulletin 1945 v 42 33). The authors comment on their findings. Their observations demonstrate the existence of plague in *Graomys griseoflavus centralis* in *Hesperomys murillus cordovensis* in *Galea musteloides leucoblephora* and in cats (*Felis domestica*). They are inclined to look on *Graomys griseoflavus centralis* as the reservoir of plague in the region studied. That animal is found in the neighbourhood of dwellings ("peridomestic") and has a preference for the nests of birds. Proof of plague in cats has been furnished and plague bacilli were cultivated from the bone marrow of three cats which had died spontaneously and had been buried for some time. A human case of plague developed in a man who had skinned a dead cat. W F Harvey

FOSTER, V. W. Epidemic of Plague in Region of Cajacay Peru. *Bol Oficina Sanitaria Panamericana*. 1944 Aug v 23, No. 8 696-9

MACCHIARELLO A. & URIGUEN D. Experimental Plague in Guinea Pigs - Inoculated with *Pastorella pestis* of Ecuadorian Origin. *Puerto Rico J Pub Health & Trop Med* 1944 June 577-601

The greater part of the argument of the authors may be said to centre round the definition of bacillary virulence. It is reasonable to contend that the definition should take into account, at least, invasive capacity and toxic effect. These may indeed, be to some extent interdependent, but must also be considered as capable of differing quantitatively. In this investigation, strains of plague from the Andean region were tested on guinea-pigs and the results are contrasted with the pathological findings described for strains from other countries. Several interesting features of the Andean strains are brought out both in experiment and discussion. They are highly invasive and peculiarly pneumotropic. Characters on which the authors insist for their strains are that they belong to that rare group for plague the S and not the R form, that although they are highly invasive and spread through the body they are of low toxicity and that the degree of invasive power becomes fixed at a limit which cannot be increased by further serial passage. It is rather paradoxically the very mildness of plague in the Andean regions that allows time for more frequent production of secondary pneumonic plague. The authors believe that the characters which they describe so far as they are limited to Ecuadorian strains represent "a phenomenon dependent on their peculiar antigenic structure" and are due to dissociation of the two main qualities which constitute virulence—invasiveness and toxicity. The lesions peculiar to Ecuadorian plague strains on inoculation into guinea-pigs are —(1) great involvement of the pelvi-aortic glands, and (2) pulmonary lesions especially of the necrotic type. W F Harvey

CHOLERA

CHOLERA

RANTA I E & DOLMAN C E A Mouse Protection Test for Cholera-Vaccine
Canadian J Pub Health 1944 Dec 1 35 No 12 473-80

Pfeiffer's phenomenon has long been used for the
but is undoubtedly very cumbersome
Bulltin 1940

Pfeiffer's phenomenon has long been used for the assay of immunizing power but is undoubtedly very cumbersome. Discovery of the fact by GRIFFITHS [this *Bulletin* 1942 v 39 764] that the addition of mucin to an immunity testing dose of living cholera vibrios greatly increased their virulence for mice furnished the necessary clue to simplification of the test. It is based upon the analogy—admittedly a loose one—between *V. cholerae* septicæmia in mice and human cholera but is at least no more fallacious than many biological tests current in vogue in other fields. It is certain that the phenol killed vaccines of the authors [this *Bulletin* 1943 v 40 540] inoculated subcutaneously in human beings do cause the development of circulating antibodies capable of conferring passive protection upon mice. In the elaboration of the test an important point has been further elucidated namely that of the protection conferred by 1-dose 2-dose and 3-dose immunization respectively. The conclusion has been reached that a spaced 2-dose inoculation in mice is much better than a 1-dose and that a spaced 3-dose immunization is not significantly better than one by two doses only. As the test involves immunization by the intraperitoneal route and testing by the same route it was necessary to meet the criticism that the immunity developed might be a purely local and not a systemic (humoral) immunity. This criticism has been met for example by the experimental demonstration that mice which had received their injections of vaccine subcutaneously showed as good protection against 5 and 10 m.l.d. of *V. cholerae* administered intraperitoneally as did similarly-challenged mice which had been vaccinated by the intraperitoneal route.

Another finding of considerable importance concerning the test is that to incorporate a variety of antigens, it is essential to use a certain amount of adjuvant.

Another finding of considerable importance is that a variety of antigenic strains in current commercial vaccines is that a degree of Inaba-Ogawa cross-protection in mice sufficiently high to eliminate the need for challenging with both type strains exists and that presumably a vaccine of either strain would also produce some immunity against the other. It must not be assumed however that type specific O antigens play no part in mouse protection. In the experimentation carried out the testing strain used was Ogawa *V. cholerae* whose virulence was maintained by successive isolations from mouse heart blood.

The authors do not recommend keeping cholera vaccines beyond two years and put forward their proposals for adoption of a conventional test of all cholera vaccines before release for use in the following terms — The arbitrary standards of antigenic potency recommended are that each vaccine should be tested by the method described on not less than 30 mice one half of which are subsequently challenged with 5 m.l.d. and the other half with 10 m.l.d. of mucinized vibrios. Of the former groups 100 per cent and of the latter group at least 80 per cent should survive. The method of immunization referred to was that of two doses 0.25 and 0.5 cc. of a 1:5 dilution of vaccine containing 8 000 million vibrios per cc. at an interval of one week. It had been found originally that 1 m.l.d. of mucinized vibrios was consistently represented by 0.5 cc. of a 1:1000 dilution of the standardized suspension

11 F Harvey

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

MARKELL, E. H. Intestinal Parasite Infections in a Naval Hospital in New Zealand. *U.S. Nav. Med. Bull.* 1945 Jan. v 44 No 1 65-8.

The patients [presumably all Americans] belonged to the Navy and Marine personnel, and a few soldiers who were admitted to a Naval Mobile Hospital in New Zealand having come from all parts of the South Pacific area more than 80 per cent of them represented random samples of patients admitted to that hospital. Specimens of faeces were taken as a rule without regard to the condition of the patients.

Fresh coverslip preparations were examined in the case of all liquid or mushy stools, one unstained and one after adding D Antoni's iodine [this *Bulletin* 1938 v 35 455] which was found better than Lugol's or Gram's solution. The flotation method of FAUST *et al* [ibid 1939 v 36 144] was used and smears of the deposit were stained with D Antoni's iodine films stained with iron haematoxylin were also prepared from each specimen of faeces.

Altogether 2,388 stool examinations were made on 1,371 patients. Intestinal parasites were found in 373 (28 per cent.) of the patients.

The author estimates from the observations of SAWITZ and FAUST [ibid 1942, v 39 765] that he found 52 per cent of the *Entamoeba histolytica* infections 65 per cent of the amoebic infections and all infestations with hookworms *Trichuris* and *Ascaris*. The percentages of patients harbouring various parasites and saprophytes are shown in a Table.

E. histolytica in 8.09 hookworm in 1.46
Trichuris in 2.12 *Giardia intestinalis* (G lamblia) in 1.46
Isospora hominis in 0.37 and *Enterobius vermicularis* *Hymenolepis nana* and *Taenia saginata* each in 0.07 per cent. Since the incidence of hookworm and amoebiasis was about double that occurring in the U.S.A. many infections were probably acquired in the South Pacific area and this is supported by the fact that hookworms were found in men from the northern States of the U.S.A. who had not lived in hookworm endemic areas before going overseas. *Isospora hominis* was found in five men four had no symptoms but the fifth had dysentery for over a month and no other cause for it was found. Most of the men had been taking mepacrine and this may explain the low percentage of *Giardia* infections.

J F Corson

BOSE A \ GROSH J H & RAKSHIT P C A Butyl Acridine Derivative in Intestinal Giardiasis. A Preliminary Note. *Indian Med. Gaz* 1944 Dec v 79 No 12 595-6

Three cases of giardiasis were treated with a butyl-acridine compound 2-chloro-7 methoxy-5 (8-diethylamino-butyl) aminoacridine which was being tried also at that time in human malaria [see above p 444]. The patients, two adults and a child of 5 years of age had suffered from various alimentary disturbances—indigestion diarrhoea colic &c. The drug was given by mouth three times a day for five days in doses of 30 mgm for the adults and 15 mgm. for the child. The stools were examined frequently for several weeks afterwards with negative results and no relapse occurred within an observation period of six months. The patients improved in health and were regarded as cured.

J F Corson

RELAPSING FEVER AND OTHER SPIROCHAETOSSES

DIXON K C & FULLER, W The Annular Forms of *Spirochaeta persica* J Roy Army Med Corps 1945 Jan, v 84 No 1 31-2.

The main interest of this note is the record of the occurrence of spirochaetal relapsing fever among troops in Cyprus about nine days after bivouacking in caves infested with *Ornithodoros tholozani*. It was generally believed in rural areas in Cyprus that bouts of fever followed the bites of ticks. The causative organism has been transmitted to guinea-pigs and is almost certainly *Spirochaeta persica* which is widespread in the Levant.

The annular forms are described by the authors as consisting of motile endoplasm rotating inside an ectoplasmic envelope. E Hindle

WOLMAN M Observations on the Value of Treatment in Louse-borne Relapsing Fever East African Med J 1944 Nov v 21 No 11 336-40

A comparative study of 311 unselected cases of louse-borne relapsing fever in Ethiopia.

The cases were divided into three groups one group was treated with 0.60 gm Neo I C I (an Italian neosalvarsan preparation) on admission and after two days with bismuth intramuscularly (Salbiolo containing 0.06 gm in a 1 cc. ampoule) the second with human convalescent serum and the patients of the third group received only symptomatic treatment.

The salvarsan bismuth treatment reduced the number of true relapses and lengthened the interval between the first and second attack but it did not reduce the mortality rate or shorten the first attack or reduce the number of non-specific rises in temperature [that is rises in temperature but with negative blood findings].

The results confirm the general opinion in Ethiopia that specific treatment of this disease has little if any value. E Hindle

CROSS R. M. Penicillin in Weil's Disease. Lancet 1945 Feb 17 211-12.

An airman was admitted to hospital with sore throat headache and general pains of three days duration his temperature was 100°F pulse rate 130 the leucocyte count 18 000 per cmm. with 79 per cent of neutrophils. Haemolytic streptococci were cultured from a throat swab.

During the next two days he had marked generalized muscular tenderness and on the 5th day of illness he had epistaxis slight jaundice and a few purpuric spots were seen on his chest. His urine contained albumin and bile granular casts and many red cells but there was no growth in culture media. Weil's disease was diagnosed and his blood was inoculated into a guinea-pig and blood serum sent to the Wellcome Research Laboratory for agglutination tests. During the next four days he had hiccup and frequent vomiting and his condition became much worse the serum bilirubin was 12.5 mgm per 100 cc. and the blood urea rose to 320 mgm per 100 cc. His cerebrospinal fluid contained 0.04 per cent of protein, normal globulin chlorides 760 mgm. per 100 cc. and the W R. was negative gamboge and Lange tests normal and the Van den Bergh test gave an immediate direct reaction.

Specific (*L. icterohaemorrhagiae*) antiserum was given—20 cc i.v. on the 9th day of the disease and 10 cc. i.m. daily on the following days up to a total dose of 60 cc. but his condition remained serious with at times delirium and incontinence. After many examinations his urine now showed leptospires.

for the first time the guinea pig died 10 days after inoculation and an autopsy showed jaundice and multiple haemorrhages in the lungs and leptospirae were found in its urine.

He was now (14th day) given sodium penicillin by slow intravenous drip after 24 hours (120 000 units) no leptospirae could be found in his urine. The report of the agglutination test was 1/10 trace 1/30 positive 1/100 positive 1/300 trace further dilutions negative.

The patient gradually recovered but had microcytic anaemia (red cells 3 740 000 haemoglobin 9.5 gm.) the blood urea returned to normal 10 days after treatment with penicillin was begun. Altogether 800 000 units of penicillin were given over seven days.

The curative action of penicillin on this strain of *L. icterohaemorrhagiae* was confirmed in a controlled experiment with guinea pigs. J. F. Corson

YAWS

LaFEVRE Ira D. Jr McDERMOTT K. F. & VEDNER, R. B. Yaws Survey on Nanumea Atoll. *U.S. Nav. Med. Bull.* 1944 Oct. v 43 No 4 739-41

The authors examined 149 natives of the island of Nanumea in the Ellice Islands, their aim being to discover the nature and appearance of the primary yaw for diagnostic purposes, the site and appearance of the secondary lesions and the various ages at which the Kahn test would be positive. They accepted the case histories as they had previously found them very reliable in a filarial survey and this was confirmed in the present survey. 46 per cent. of the 97 children examined gave a history of yaws and 46 per cent. of the 66 Kahn tests made in this group of 97 children were positive [presumably all the children with positive Kahn tests also gave histories of having had yaws].

The people examined were divided into (1) children under 3 years old (2) children 4-16 years old, and (3) adults over 16 years old. The primary yaw was found only in group (1) and among the younger children of group (2) secondary yaws were found mostly on the palms and soles and there were very few cases of tertiary yaws. The figures of findings under various sub-heads—number examined history of yaws clinical yaws present or absent Kahn test positive or negative &c. are tabulated. About 50 per cent. of children under 16 years of age showed evidence of yaws but the highest proportion (71 per cent.) of Kahn positive reactions was found among the adults. J. F. Corson.

I. WHITEHILL R. & AUSTRIAN R. The Treatment of Primary and Secondary Yaws with Penicillin. A Preliminary Report. *Bull. Johns Hopkins Hosp.* 1944 Oct. v 75 No 4 233-40

II. — & —. Treatment of Yaws with Penicillin. *Bull. U.S. Army Med. Dept.* 1945 Mar. No 86 84-91

I. Seventeen cases of active primary and secondary yaws in natives of Fiji were treated with penicillin. 11 of the patients had had no previous treatment with arsenical drugs while the other six had relapsed after such treatment. In 18 cases the Kahn test was positive before treatment with penicillin, and spirochaetes were seen, by dark ground illumination in all cases.

Penicillin was given intramuscularly in doses of 15 000 units every four hours day and night, for 5-6 days. The solution in normal saline, contained 10 000 units per cc. Fourteen patients received 450 000-500 000 units while the

naming three patients had 250 000 200 000 and 100 000 units respectively during the first 16 hours the total dosage varied from 50 000 to 90 000 units and at the end of this period all lesions were healing and except one they had completely healed within three weeks ulcers and granulomata several centimetres in diameter healed within a week.

Sporochaetes were not seen by dark-ground illumination after 16 hours from the beginning of treatment in 16 of the cases while in the remaining case one sporochaete was seen at 16 hours none at 40 hours.

The Kahn test remained positive in all cases during the short observation period of two to seven weeks.

As healing took place as quickly and completely after the smaller dosage given to three patients the authors think that this dosage is probably sufficient but that further study of larger numbers and for a prolonged period of observation is necessary before final conclusions on this and other points can be drawn. This is an account of the same 17 cases of yaws and its contents are substantially the same as in the preliminary report. In an addendum however the authors state that further observations on these 17 patients together with notes on 25 additional cases have been submitted for publication and they give their conclusions which were similar to those in the preliminary paper.

J F Corson

LEPROSY

BERNANDEZ J M. M. Importancia das reações imunológicas no exame das crianças comunicantes de leprosos. [Significance of Immunological Reactions in Examination of Child Contacts of Lepers.] *Rev Brasileira Leprologia* S Paulo 1944 Sept. v 12, No 3 201-13 2 figs. on 1 pl. English summary

H W WADE has classified the results to individuals exposed to leprosy as follows —

- 1 The bacillus fails in its attack and is eliminated—a common event.
- 2 The bacillus enters but is checked and produces no symptoms afterwards according as resistance is maintained or breaks down the infection may be eliminated, or remain latent or give rise to symptoms.
- 3 Localized signs are produced which may persist without further development or may spontaneously disappear.
- 4 Clinical signs of a benign nature may ensue—nervous leprosy.
- 5 Clinical signs of a serious nature may ensue—lepromatous or cutaneous leprosy.

R. COCHRANE notes that children acquiring infection in infancy may go on to (1) Progressive disease. (2) Do the same when resistance subsequently breaks down after a period of latency. (3) Show a stationary condition with a lesion checked and inactive but evident. (4) The lesion may disappear completely.

After these preliminary statements the author goes on to describe the lepromin reaction and its interpretation—a positive indicating that the subject has been infected with the organism and is sensitized and that resistance is being offered so that the prognosis is favourable. *Per contra* children reacting negatively call for rigorous supervision. It must be remembered however that infants though living in close contact with lepers only exceptionally react positively under 12 months of age. If after that time and in these circumstances the reaction is still

negative careful watching is called for as the child may be incubating an infection of a malignant type. In those with obvious manifestations and a positive reaction the prognosis is favourable. In other words a positive reaction indicates resistance. It is useful also retrospectively in that a healed cicatrized lesion if leprosy, will react with a local erythema. Further it will reveal hidden lesions as in a skin apparently normal a subcutaneous injection of 0.5-0.75 cc. may in 24 hours show up a number of erythematous blotches quite unsuspected.

We may sum up the information derived from the lepromin test as follows —

I. *Patient showing active lesions*

- (a) *Lepromin reaction positive* Prognosis good strict vigilance not needed.
- (b) *Lepromin reaction negative* Make bacteriological examination. If the organisms are not found, watch the case carefully and repeat the test periodically. Anyway it is advisable to start treatment with chaulmoogra.

II. *Patient showing residual lesions*

- (a) *Lepromin positive* As in I (a)
- (b) *Lepromin negative* Watch case carefully repeat the test.

III. *Patient showing no obvious lesions*

- (a) *Lepromin positive* Note signs of early healed lesions. As in I (a)
- (b) *Lepromin negative* Careful watching repeat test periodically. Start specific treatment with chaulmoogra if clinical signs appear. If the reaction continues negative, give a guarded prognosis.

[See also this Bulletin 1935 v 32, 862 1939 v 36 892 1940 v 37 335 1941 v 38 703 1942 v 39 226 227 696 1943 v 40 245 316-17 648 786] .

H. Harold Scott

DOE SANTOS NEVES E. Mais uma tentativa de tratamento do doente de lepra.
[Another Suggested Treatment of Leprosy] *Rev. Brasileira Leprologia*
S Paulo 1944 Sept v 12 No 3 247-51

This short article is of the nature of a preliminary note with brief remarks on five cases of leprosy which had failed to respond to the customary treatment with chaulmoogra or which had not had any previous treatment but which showed marked improvement and negative results to examinations for *Mycobacterium leprae* after the new treatment.

The idea arose from the report of a patient under Dr. Etcheverry in Buenos Aires with definite signs of leprosy and bacteriologically positive who after an attack of jaundice with desquamation appeared to be cured of his leprosy [no reference is given]. The author then argued as follows: Vitamin A is the anti-infection vitamin and its absorption is facilitated by bile. Carotene is transformed into vitamin A in the liver. *Mycobacterium leprae* is a resistant organism, as evidenced by its long latency and difficulty of inoculation into animals: abuse of remedies even chaulmoogra is prejudicial. Spontaneous cure (i.e. cure by the unaided efforts of nature) sometimes takes place. Hence a rational mode of treatment would be to assist nature by administration of vitamin A and a cholagogue. The author therefore started by using Decholin, a product of the Riedel laboratory and vitamin A from the Dahr laboratory. Later he used a cholagogue and carotene and carotenoid provided by the local laboratory. Injections were made intramuscularly three times a week. The results recorded are very striking. [But unfortunately nothing is said of the dosage nor the length of time for which the treatment was maintained, nor of any follow up of patients to see whether the improvement or cure with absence of bacteria was permanent.]

H. Harold Scott

SILVEIRA L. M. Patogenia do mal perforante plantar [Pathogeny of Perforating Ulcer of the Sole] *Rev Brasileira Leprologia* S Paulo 1944 Sept v 12, No 3 255-66 13 figs on 6 pls.

Perforating ulcer of the sole has (theoretically according to the author) been ascribed to nerve or vascular lesions to dyscrasias or certain intoxications but it is difficult to say what part each of these may play in the pathogeny of plantar ulcers. Briefly the author will not have anything to say for any of them except in so far that the initial phenomenon is loss of sensation of pain. That being so any wound goes unperceived and consequently untreated and infection is superadded after which destruction of tissues soft tissues and even bone proceeds apace. If seen in the early stage the ulcer should be treated on the lines proper to any wound by cleanliness and rest and thereafter careful observation to see that the healing does not break down owing to the analgesia. If the patient does not come for treatment till later surgical intervention will be necessary and, in many cases amputation. There are photographs showing the condition before treatment and the results of surgery. *H Harold Scott*

LINHARES Hermínio VII Contribuição ao estudo da lepra murina. [Contribution to the Study of Murine Leprosy] *Rev Brasileira Leprologia* S Paulo 1944 Sept. v 12 No 3 217-44 [154 refs] English summary

This article is a contribution to the study only in so far as it summarizes our present-day knowledge of the subject of murine leprosy and its similarities to the human disease. The author deals with the organism Stéfansky's bacillus its characters and the results of attempts at culture of material from different sources and on different media and briefly discusses the relations between the human and rodent disease concluding that Hansen's and Stéfansky's organisms are one and the same but that epidemiologically there is no connexion between human and murine leprosy nor is there any proof that the bacilli exist saprophytically in the soil and produce their respective diseases by penetrating cutaneous lesions. All the statements made are supported by references to the literature and a full and useful bibliography of 154 references is given. The only original statement is a note on a trial of penicillin in the treatment of murine leprosy the results are not conclusive and so far are not encouraging. *H Harold Scott*

HELMINTHIASIS

Niño F. L. Papel de los helmintos en las llamadas apendicitis verminosas. [Role of Helminths in the So-called Verminous Appendicitis.] *El Día Médico* Buenos Aires 1944 Nov 6 v 16 No 45 1371-2 6 figs

The term verminous is here used in its strict etymological sense of associated with worms. Photomicrographs are reproduced showing cross sections of the appendix with worms in the lumen and inflammatory changes in the wall of the viscus. Professor Niño refers to his address in 1937 when he recorded that of 1018 appendices which he had examined, twenty of them (1.96 per cent.) contained helminthic parasites and thirteen of these were *E. vermicularis*. In the next seven years he examined 745 more and found another 36 (4.8 per cent.) giving a total of 56 with worms among 1763 appendices examined 3.17 per cent. Fifty of the 56 positive were *E. vermicularis* four were segments of *Taenia saginata* one had ova of *Trichuris trichiura* and one

reality cough dyspnoea tachycardia, palpitations pruritus, etc. are more frequent. Two of our patients were at first thought to be suffering from measles.

"13. Thoracic pain which is generally localized to the vicinity of the parasite is an early symptom. It is transient and probably not due to obliterative pleuritis. Pleural adhesions form late.

"14. Sudden expectoration of a large amount of clear salt tasting fluid is diagnostic of the rupture of a simple cyst.

15. There are no signs pathognomonic of hydatid disease indeed, in the case of simple cyst the signs are notable for their absence, and the first abnormality to be detected may be due to the onset of complications. The great majority of simple hydatids are symptomless.

"16. The disease is apt to be associated with other conditions such as pulmonary tuberculosis silicosis pneumonitis etc.

17. A striking feature of the cases we have seen is that so few had hydatid cysts in viscera other than the lungs. Bilateral cysts are not uncommon.

"18. The dangers of aspirating an hydatid cyst, for purposes of diagnosis or treatment are not sufficiently realized. The fact that aspiration can sometimes be done without danger does not justify its use under any circumstances.

19. The disease is generally mistaken for pulmonary tuberculosis atypical pneumonia, new growth tuberculous pleurisy with effusion or pneumothorax of unknown cause.

"20. The patient who harbours an hydatid cyst must either discharge the parasite or die as a result of it.

"Part III.—Treatment.

21. The relative merits of surgical and expectant treatment are reviewed.

"22. Neither drugs nor X-rays can destroy the parasite in the lung and even if success could be achieved in these ways a foreign body would be left in the tissues. Suppuration would ultimately be inevitable.

"23. Statistics are available to indicate the chances of expectoration of the parasite under different conditions but no man can predict the fate of any individual patient. He who harbours an hydatid cyst stands beneath the sword of Damocles.

"24. A survey of the literature indicates that surgical opinion, the world over is in favour of removing the parasite at the earliest possible moment. The mortality and morbidity of operative removal is much lower than that of conservative treatment.

25. The safest way to enucleate a simple cyst is to treat it as a lung abscess—that is, to localize the lesion accurately and to create pleural adhesions (if these are not already present) before traversing the pleural membranes. The fact that surgeons whose experience of this disease is great make light of the dangers of the open pleura does not, in our opinion, entitle the tiro to follow their example. The technique of various operative procedures is described.

26. If the parasite has produced permanent pathological changes in the parenchyma of the lung or in the bronchial tree, it is manifest that simple enucleation of the cyst will not cure the patient. The operation will avert the dangers of anaphylaxis rupture haemorrhage etc. but leave the patient to endure the ravages of pulmonary suppuration.

"27. In a selected group of cases the treatment of choice is lobectomy. The arguments in support of this statement are catalogued, and the results so far achieved are such as to justify further investigation of this matter.

ZIZAROR, J & SZUCS M. M. *Echinococcus Cyst of the Heart* *Amer J Roentgenology* 1945 Jan. v 53 No 1 15-19 3 figs [11 refs]

KOURI P. Tercer informe en relación al *Inermicapsifer cubensis* (Kouri 1939) [Third Communication on *Inermicapsifer cubensis*] *Rev Med Trop y Parasit Habana*. 1944 Sept.-Oct Nov Dec. v 10 Nos. 5-6 107-12 [23 refs]

The author outlines the history of this cestode. Some 11 species of the genus have been found in rodents and African Hyracoidea but *I. cubensis* described by KOURI and BAER, is the first American species to be recorded. Baer suggested that it was introduced to South America from West Africa. Kouri here decides that *I. cubensis* is synonymous with *Raillietina cubensis* *R. konradovits* and *R. loechesalavesi*. He also places all the South American equatorial species of *Raillietina* in the species *R. demerariensis* (i.e. this species is synonymous with *R. quilensis* *R. lusaleoni* *R. equatoriensis* *R. brumpti* and *R. leoni*) [see also DOLLFUS this *Bulletin* 1940 v 37 214 and 1941 v 38 112]

The first human infestation with *I. cubensis* was discovered in 1930 by Hernández LOECHE and Alavez OLMO by 1940 some 32 cases had been described [KOURI and RAPPAPOORT this *Bulletin* 1941 38 113] in the paper under review Kouri reports more than 70 cases up to 1944. The parasite, he says, most frequent in the provinces of La Habana (more than 70 cases Matanzas (8 cases) and Pinar del Río (5 cases). A piece of a cestode received in 1944 by the author from Lara State Venezuela is suspected to be *I. cubensis*. Most of the infested subjects have been children between one and two years old. The youngest was aged 5 months. Three were aged 9-11 and two 18-35. All were whites except one negro. Usually, each subject harboured only one cestode but three expelled two and one expelled four. Usually, the cestode is expelled spontaneously after a few months and it readily yields to simple purges or anthelmintics. This fact the tender age of most of the subjects and the poor resistance of the proglottids and egg capsules to external conditions (they disintegrate outside the host in 24-48 hours) suggest that man is not a favourable host. That the normal host is a wild or domesticated animal and that the intermediate host is abundant so that the eggs are eaten in the short time available before external conditions render them non viable. Expeditions to the infested areas in Cuba failed to reveal the parasite in the 658 animals examined most of which were mammals (oven sheep goats pigs horses cats dogs ferrets Cuban rats bats and frogs) nor was an intermediate host discovered among the acarid, insects and crustacea examined. Nor have PÉREZ VIGERAS and ROCCELIO ARENAS in the course of their examination of large numbers of Cuban animals found this cestode. The search for the normal and intermediate hosts provided much other information about Cuban parasites. An experimental attempt to infest man with the gravid proglottids of *I. cubensis* and with plerocercoids of *Diphylobothrium mansoni* were both negative. Most of the animals examined were heavily parasitized by cestodes nematodes and protozoa, but the bats, frogs and ferrets were free from intestinal helminths. The unknown life history of *Platynosomum fastosum* of the liver of the cat which is common in Cuban cats was studied and also that of *Diphylobothrium mansoni* which occurs in 100 per cent of Cuban cats in certain rural areas although it is absent from the town cats.

None of the 366 rats examined harboured *Trichinella spiralis* which has not yet been reported from Cuba but these rats did not come from slaughter-houses
(233)
G. LaPage

[June 1945]

Tropical Diseases Bulletin.

FERRO-LUZZI G Il problema dell'anchilostomiasi in Eritrea. [Ankylostomiasis in Eritrea.] *Boll. Soc. Ital. di Med. e Igiene Trop* (Sex. Eritrea) 1944 v 4 No. 2 369-75 English summary (8 lines)

Up to the present states the author the problem of ankylostomiasis has not arisen in Eritrea any cases there might be and they were rare were imported. Now however owing to the movement of troops, immigration of agricultural and industrial workers of natives from neighbouring districts the passage of coloured troops from the country are becoming endemic loci of infection prevails parts of the country are becoming endemic loci of infection.

The author has made examinations of very small numbers in three places within 15 kilometres of Asmara he used the Willis technique. In one Amba Derbo he examined 13 apparently healthy persons and found nine passing the ova in another Gherem 8 kilometres from the last he found 16 positive out of 30 and in a third Beless some distance from both these one positive out of ten, that is 38 positive in 53 persons examined. He calls the passage of ova was a mild degree of eosinophilia (number not given) and how far this was due to the hookworm is conjectural because other helminth infestations—*Enterobius Ascaris* and *Tania*—are very common among Eritreans. In order to prevent the condition becoming ineradicable the author pleads for the usual methods of prevention to be undertaken without delay. H. Harold Scott.

JOHNSON P A G Filariasis. Clinical Findings in 189 Cases. *U.S. Nav. Med. Bull.* 1944 Nov. v 43 No. 5 950-54

From July to November 1943 observations were made on 189 cases of filariasis in United States Marines who had returned from the South Pacific area to the Marine Corps Base at San Diego, California. The men had served in Samoa, Wallis Island or in both these places. The observations are presented in a table which shows the relative frequencies of the chief symptoms and signs, the periods of service with and without symptoms and the number of days in hospital and on leave.

As regards prognosis it was found that the longer the time spent in the U.S.A., the greater was the improvement. It was very marked in patients who had been in the U.S.A. for over 107 days. Great importance is attached to special attention being given by medical officers early in the disease particularly for its beneficial psychological effect on the patient. Rest in bed, light duties and an explanation to the patients of their case assured them as to their ability to work and reduced their requests for prolonged hospitalization. J. F. Coxon.

YEXNER, R. B. Filarial Problem on Nanumea. *U.S. Nav. Med. Bull.* 1944 Nov., v 43 No. 5 955-63

Nanumea, the most northern of the Ellice Islands was occupied by American Marines on September 4th 1943. The native population of 800 had been removed in August to the neighbouring island of Lakena, 24 miles away which had been largely used by the people of Nanumea for farming. The Marines had previously lived in Samoa for many months so investigations on filariasis were limited to observations on the local mosquitoes and on the natives. Mosquitoes and their larvae were collected and notes were made of the conditions under which they lived. The natives were examined by questions, physical examination and by taking blood films. The survey lasted for a month and produced two unexpected results. (1) there was more filariasis, especially in a chronic stage than was expected. (2) both the Marines on Nanumea and the natives on Lakena were

providing breeding places for mosquitoes. As the natives had lived in other places which were endemic areas of filariasis there was no proof that any of them had acquired the disease in these islands.

The adult mosquitoes found were *Aedes aegypti* and *A. scutellaris pseudo-scutellaris* in about equal numbers. Their larvae were found in rain water in barrels coconut shells hollow tree stumps &c. in Nanumea while in Lakena they were chiefly found in pits used for growing an edible root called taro (*Colocasia esculenta*). Larva of *Culex annulirostris* were also found in both islands. Staining of blood films was not very successful at first but of 65 well stained films microfilariae were found in 33. Antimosquito measures suitable to the local conditions were recommended to the authorities concerned.

FRD E E ST AMANT L S & BROMBERG L. Studies on Filariasis in the Samoan Area. *US Nav Med Bull* 1945 Jan. v 44 No 1 1-20, 9 figs
J F Corson
& 1 graph

The authors made various observations and experiments on filariasis in the Samoan Islands from April 1943 to February 1944. They recognized seven species of mosquito (there are said to be 10) *Aedes scutellaris* var *pseudoscutellaris*, *A. aegypti*, *A. samoana* (kochi?), *A. vexans*, *Culex fatigans* (quinquefasciatus), *C. annulirostris* and *C. sitiens*. Caught specimens of those except *C. sitiens* were dissected for larvae of *Wuchereria bancrofti* with the result that they were found only in *A. scutellaris* var *pseudoscutellaris* and *C. fatigans*. 2.9 per cent of 6634 specimens of the former species and 7.4 per cent of the latter had larvae but in *C. fatigans* they were not beyond the 7-day stage of development. More than 15 per cent of the former species had larvae in the infective stage many had dual or triple infections.

Laboratory bred mosquitoes of these two species were given a single feed on the same person. *A. scutellaris* var *pseudoscutellaris* showed infection in over 80 per cent and of those which survived for 15 days 80 per cent had larvae of the infective stage. *C. fatigans* showed infection in 29 per cent but of 25 which lived for 15 days only one had larvae of the infective stage. Early larval stages were found in feeding experiments with *A. aegypti* and *C. annulirostris* but no infective stages were seen.

The habits of the adult mosquitoes were observed with results in agreement with those of previous workers [see O CONNOR this *Bulletin* 1923 v 20 5 and 891 BUXTON *ibid* 1927 v 24 941]. The two commonest mosquitoes are *A. scutellaris* var *pseudoscutellaris* and *A. samoana* the former bites by day breeds in a great variety of casual collections of water—coconut shells tin cans rot-holes &c and does not fly far (rarely more than 100 yards) from its breeding place the latter bites at night and breeds only in the axils of the taro mat grass and pandanus plants.

The authors recommend antimosquito measures and segregation of troops from infected natives as well as native villages as far as may be practicable and in accordance with local conditions.

GLAUSER F. Filariasis in Returning Marines. *US Nav Med Bull* 1945 Jan. v 44 No 1 21-6 4 charts
J F Corson

The case histories of 172 Marines who had served in the Samoan Islands were reviewed, the men themselves examined, and some treated. The inquiry was mainly a numerical analysis and included such details as the number of men who developed symptoms while still on the islands the incidence in individual islands the number of months between landing and the first appearance of symptoms the time of day or night when symptoms first appeared the

mode of onset and the part of the body which first showed signs, and the results of physical examination. Most of the observations agree with those made by other workers on Service men who have returned to America from South Pacific islands. Allergic signs, such as localized itchy swellings, were present in 32 and spindle-shaped swellings were seen in the linear aspect of the forearm and over the calf. The author found great variation in all the points examined. He concluded that symptoms were exaggerated and that psychic trauma appeared to play a considerable part. The disease was not disabling and did not interfere materially with duty and hospitalization was unnecessary. recurrences were frequent but not important. The disease caused neither impotence nor sterility and there seemed to be no probability of elephantiasis developing. No form of treatment was effective (see also this Bulletin 1944 v 41 303 304 880 and 956 *ibid* 1945 v 42, 53) J F Corson.

ZUCKERMAN S S. & HINNARD J S. Clinicopathologic Study of Early Filariasis with Lymph Node Biopsies. *J S Am Med Bull.* 1945 Jan., v 44 No. 1; 27-38

The authors excised lymphatic glands in 62 cases of filariasis in Samoa (the patients probably belonged to American military personnel though this is not definitely stated). The glands were removed from patients in various stages of the disease and they had various anatomical relations with areas of acute lymphangitis. The histological picture seen in sections was fairly constant, but the authors classified the cases into four groups based on histological variations: (1) adult filariae present inside or outside the node (2) no adult filariae present but there was dense eosinophilic infiltration (3) neither adult filariae nor eosinophilic infiltration present but the gland was anatomically connected with acute lymphangitis (4) like (3) but without anatomical connection with acute lymphangitis which however was present elsewhere in the body.

The sections showed marked hyperplasia of the reticulo-endothelial cells and a prominent hyperplastic and obliterative endolymphangitis "even in Group (4). This suggests that the pathological changes represent a generalized reaction to the toxic or metabolic products of the worm itself not to its disintegration products. There was much variation in the degree of eosinophilic infiltration its presence in Group (1) where it was intense and its absence from Groups (3) and (4) suggest a direct association with the presence of filariae. There was no evidence that lymphangitis was due to bacterial infection. The authors concluded that biopsy is unnecessary for diagnosis in most cases but is useful to confirm a diagnosis in clinically atypical cases. J F Corson.

HARTY P H. Contribution to the Histopathology of Filariasis. *Am J Clin Path.* 1944 Jan., v 14 No 1 34-43 8 figs

In the abstract of this paper published in this Bulletin 1944 v 41 855 line 19 the sentence "There is no necrosis when the microfilariae are intact" should read "Necrosis was never seen when the filariae were intact." Throughout the paper the changes described are those brought about in connexion with adult worms.

GOLDMAN L. American Onchocercariasis. *Arch. Dermat & Syph* 1944 Dec., v 50 No 6 385-43 6 figs. (19 refs.)

This paper is a useful general account of onchocerciasis in America only which should be useful to those who are unable to consult the more detailed accounts in standard textbooks of tropical diseases. There are two good photographs

of cross sections of *Onchocerca* nodules. Among the diagnostic methods briefly discussed is the method of feeding non infested Simuliid flies upon persons suspected of having onchocerciasis and later examining the flies for microfilariae. The author's brief comparison of onchocerciasis with infestations with *Wuchereria bancrofti* will be useful to those who are looking out for these two infestations at the present time among Allied troops in the areas where these diseases occur.

G Lapage

GAASE. A. Der Trichinellen Antikörpernachweis im Liquor cerebrospinalis und der Nachweis von Trichinellentoxin in der Hirnsubstanz durch die Komplementbindungsreaktion. [The Demonstration of *Trichinella* Antibodies in the Cerebrospinal Fluid and the Demonstration of *Trichinella* Toxin in the Brain Substance by means of the Complement-Fixation Reaction.] *Munch med Woch* 1943 Oct 22 v 90 No 42/43 612.

The author records the history of a patient who developed 18 days after eating pork, a haemorrhagic diarrhoea and swelling of the eyelids. There was 12 days later an eosinophilia of 50 per cent. and a complement fixation test done about 15 days after the first appearance of symptoms was positive on the 39th day it was strongly positive. The condition was complicated by tonsillitis with fever marked headache in the right temporal region some deafness and impairment of sight the patient became stuporose with stiffness of the neck and positive Kernig and Brudzinski signs. Lumbar puncture removed a clear cerebrospinal fluid which gave a strongly positive test with *Trichinella* antigen. The patient died but death was attributed to generalized sepsis and not to trichiniasis. Haemolytic streptococci were recovered at autopsy from the swollen spleen and there were metastatic abscesses in the heart muscle and kidney with a chronic perietal endocarditis and haemorrhagic infarcts in the spleen and left kidney. *Trichinellae* were found in sections of the muscles of the neck, upper arm thigh and in the diaphragm but not in the oedematous brain substance which was examined both by digestion in pepsin and HCl and by crush preparations.

Gaase fed guinea pigs with the brain substance of this human subject and even two days later the guinea pigs gave a positive complement fixation reaction to *Trichinella* antigen and this persisted. Earlier [see *Bulletin of Hygiene* 1943 v 18 209] Gaase had found that guinea pigs fed with trichinized meat showed a positive complement fixation reaction as early as three and five days after the feeding. He has also observed the same result after intraperitoneal injection of *Trichinella* antigen into guinea pigs without the presence in them of viable *Trichinella* larvae. He suggests that if there were any trichinellae in the brain substance of this human subject they were too few to cause any symptoms in the guinea pigs fed with it but he thinks it more probable that the brain substance contained *Trichinella* toxins and that these caused the production of antibodies so that the early positive complement fixation reaction was obtained. Gaase explains the nervous symptoms as being due to the *Trichinella* toxins. The same view has been expressed by others (BORSCH [BOSCH] H *Munch med Woch* 1931 v 78 No 11 436 and FLEISCHMANN P *Deutsch med Woch* 1930 v 56 No 16 648). The presence of *Trichinella* in the cerebrospinal fluid and brain substance has been recorded by MATOFF K *Zschr infekt Krankh Hanstiere* 1940 v 56 [no page] and FROTHINGHAM cited by SEIFERT O *Handb der pathog Mikroorganismen* 1929 v 6 Pt. 2 1011). Gaase claims that the observations here recorded afford further evidence of the value of the complement fixation reaction for the diagnosis of trichiniasis. [*cf* GAASE A. *Bulletin of Hygiene* 1943 v 18 210 and the reverse evaluation

of LIDNEWITZ F and HARMSEN this *Bulletin* 1943 v 40 935 See also other papers in the *Bulletin of Hygiene* and this *Bulletin* 1944 v 41 716]

G. LaPage.

WENDEROTH H Ueber Schäden des Kreislaufapparates bei Trichinose. [Circulatory Lesions in Trichinosis.] *Deut. Wochenschr.* 1942 Nov v 7 No 11 687-91 3 figs

Trichinella infection is common says the author in the German armies in the east of Europe because Russian pigs are heavily infested. [Before the war and probably now also Germany itself was one of the countries where trichinosis was rife.] In the present paper he deals with 58 cases 15 very severe (8 ending fatally) 28 of average severity 11 mild, and 9 showing very slight symptoms diagnosed as "rheumatism" but with eosinophilia of 10 per cent. or so. Of the changes occurring in the blood vascular system he notes increased corpuscular sedimentation rate increased pulse-rate but usually not higher than the accompanying fever would explain except in very severe cases where the toxic condition is leading to collapse and heart failure oedema is due to toxic effects on the capillaries and connective tissue. One of the most important lesions of the circulation is thrombosis cases are referred to in which this occurred in lung, mesenteric veins the sigmoid alium and the saphenous vein with pulmonary infarct. *Trichinella* was not seen in the myocardium—the heart muscle has no sarcolemma—but myocarditis with eosinophilia and round-cell infiltration is common, or focal lesions with interstitial infiltrations by lymphocytes, plasma cells and a few leucocytes or oedema of the connective tissue as in cardiac dropsy. Electrocardiographic changes—three electrocardiograms are reproduced—are explained by a widespread myocarditis of multiple small foci, which soon clear up when the helminthic infestation ceases.

H. Harold Scott

HAEMATOLOGY

MOORE C. V. VILTER, R. MURKIN V & SPIES T. D. Nutritional Macrocytic Anemia in Patients with Pellagra or Deficiency of the Vitamin B Complex. *J. Lab. & Clin. Med.* 1944 Dec. v 29 No 12, 1238-55 7 figs. [64 refs.]

This important paper describes clinical and laboratory studies in macrocytic anaemia associated with pellagra and other manifestations of vitamin B complex deficiency. From 1940 to 1943 56 patients with this syndrome were observed in the Nutrition Clinic of the Hillman Hospital, Birmingham, Alabama, and 25 of them were selected for special study.

The patients were white subjects mostly over 50 years of age males being three times as frequent as females. They all had subsisted for years on diets grossly deficient in animal protein. The clinical manifestations related mainly to the skin gastro-intestinal tract cardiovascular system and peripheral nerves. Signs of pellagra, arboflavinosis or beriberi were present in most of the patients. The skin in all cases displayed hyperpigmentation roughness and dryness but never had the fine texture and lemon tint of Addisonian pernicious anaemia. Persistent diarrhoea was almost a constant feature.

The anaemia was macrocytic and megaloblastic the initial red cell counts ranging from 1.14 to 2.33 millions per cmm. The peripheral blood and sternal bone marrow were invariably indistinguishable cytologically from those of

Addisonian pernicious anaemia. The cases differed however from the latter condition in the following respects —

(1) Free hydrochloric acid was found in the gastric juice on at least one occasion in 21 of the 25 cases. (2) The icteric index and with two exceptions the serum iron values were within normal limits. (3) Experimental evidence indicated that intrinsic factor was present in the gastric juice. Features distinguishing the syndrome from sprue were the normal faecal fat values and the absence of significant abnormalities on barium meal radiological examination.

Appropriate treatment was followed by marked clinical improvement and haematological remission. Those patients who corrected their former faulty dietary habits remained well without further treatment. Failure in this respect however resulted in relapse in 18 to 24 months.

Niacin [nicotinic acid] thiamin riboflavin calcium pantothenate pyridoxin inositol para-aminobenzoic acid and choline given together daily both orally and parenterally caused amelioration of many of the clinical manifestations of avitaminosis but exerted no haemopoietic effect.

The daily administration by mouth of 200 gm of ground beef muscle or of an 80 per cent alcoholic extract equivalent to 250 gm of beef or of crude liver extract resulted in suboptimal reticulocyte responses and eventually in moderate rises in the red cell counts. Replacement of this therapy by daily intramuscular injections of highly purified liver extracts was invariably followed by secondary reticulocyte responses and marked acceleration of red cell regeneration.

The presence of intrinsic factor in the gastric juice of two patients was demonstrated by biological assay. Samples of the patients' gastric juice added to raw beef and administered to cases of Addisonian pernicious anaemia, resulted in reticulocyte responses.

In another experiment a patient was given beef extract orally with a resulting reticulocyte response. When the beef extract was replaced by an equivalent amount of beef to which normal gastric juice had been added a secondary rise was noted. A maximal reticulocyte response and rapid red cell regeneration only occurred however when injections of purified liver extract were substituted for the earlier treatment.

The authors conclude from their experiments that the pathogenesis of these cases of nutritional macrocytic anaemia seems to depend on the existence of a prolonged dietary deficiency of extrinsic factor associated in many instances with poor absorption from the intestinal tract with or without inadequate production [but not complete lack] of intrinsic factor by the gastric mucosa. Final proof awaits the isolation and clinical trial of extrinsic factor.

The possible relationship of this form of nutritional macrocytic anaemia to sprue and to tropical macrocytic anaemia is discussed. Attention is drawn to the ease with which this syndrome may be confused with Addisonian pernicious anaemia, since patients may show intermittent achlorhydria and it is suggested that the syndrome may be more common in areas where pellagra is endemic than has formerly been realized.

[This paper should be read in the original by all investigators in this field since it breaks new ground and provides a valuable contribution to the subject.]

The invariable therapeutic success obtained with highly purified liver extracts administered parenterally is of considerable interest in view of conflicting reports on this point from India and elsewhere. It should be noted however that in the present work the liver extracts were usually given in massive dosage and that in many cases the patients had previously been on high protein and high vitamin diets.]

L. J. Davis

VOORHIES, V. W. & SLOAN F. R. Mediterranean Anemia. *J Amer Med. Ass.* 1944 June 3 v 125 No. 5 352-4 4 figs. [12 refs.]

Captain Voorhies and Major Sloan describe a case of splenomegaly and mild anaemia associated with skeletal changes, in a young man of 20 as a case of Mediterranean anaemia. The patient was born of Sicilian parents. [Unfortunately as his eyes are covered, it is impossible to judge of his mongoloid appearance and the reproductions of the X-rays are not clear enough to study the bone changes present.] The authors themselves admit that the vertical striations connecting the inner and outer table of the skull bone which is so typical a finding in this disease were not present. [The authors' diagnosis should be regarded as not proven.] *Janet Laughan.*

BAUER, J. & FISHER L. J. Sickle Cell Disease with special regard to its Non-anaemic Variety. *Arch Surgery* 1943 Dec., v 47 No 6, 553-63 [Refs. in footnotes.]

Among seven cases of sickle cell disease reported in detail, Professor Bauer and Dr. Fisher found five in whom the diagnosis had not even been suspected during life but was made at post-mortem. They emphasize the importance of recognizing that anaemia is not an obligatory sign of sickle cell disease. Serious consequences may result from circulatory stasis of the sickle cells in the small blood vessels rather than from the anaemia. Persons with the sickle cell trait are the authors consider potential candidates for sickle cell disease with or without anaemia. Many cases however of sickle cell disease are not diagnosed correctly because the sickling phenomenon is not looked for. The authors suggest that it is imperative that the misnomer "sickle cell anaemia" should be abandoned and the term "sickle cell disease" be used instead. They do not agree with WERNICKE that the sickle cell trait is of little clinical significance, but suggest that a person with this trait has one of the following chances — (a) he may have the sickle cell trait without further consequences (b) he may develop sickle cell disease as characterized by typical post-mortem changes particularly in the spleen without however any impairment of health (c) sickle cell disease may develop causing circulatory stasis in various organs which may produce abdominal or neurological symptoms pain of bones and joints and other manifestations of an impaired circulation (d) a more or less severe anaemia may develop (e) an anaemia due to a cause other than the sickle cell trait may develop (f) other constitutional abnormalities may be present which may result in ill health. Since the sickle cell trait is commonly found in American negroes the authors consider that all negro patients in both medical and surgical services (wards) should be tested as a routine for sickle cell disease and that all negroes in the armed forces should also be tested. *Janet Laughan.*

WINSOR, T. & BURCH G. E. Diagnostic Physicochemical Blood Tests in Sickle Cell Anemia. *Amer J Med Sci* 1944 Feb v 207 No 2 152-60 2 figs.

In a study of the sedimentation rate in sickle cell anaemia Dr. Winsor and Professor Burch noted that CO_2 causes a marked retardation, and oxygen a marked acceleration in the rate. The sedimentation rate is not affected to the same degree in other conditions and the authors have described simple tests making use of these phenomena the effects of O_2 and CO_2 which they consider are 88 per cent. reliable in the identification of sickle cell anaemia. For details of the method and statistical analysis of the data on which their conclusions are based reference should be made to the original paper. *Janet Laughan.*

DERMATOLOGY AND FUNGOUS DISEASES

DENENHOLZ, E. J. & CHENEY, G. Diagnosis and Treatment of Chronic Coccidioidomycosis. *Arch Intern Med* 1944 Nov. 74 No 5 311-30 10 figs. [Refs. in footnotes]

This important paper dealing with chronic coccidioidomycosis mainly from the standpoint of clinical pathology, should be read in the original. The authors emphasize the bizarre character of the symptomatology of the disease and stress the value of accessory aids in diagnosis. They studied a series of 44 cases diagnosed as coccidioidomycosis, in only 14 of which however was the diagnosis confirmed mycologically. These cases are used to illustrate the authors' seven steps in diagnosis which are as follows:—

(1) *History.* Exposure to infection in a known endemic area of the disease or the record of an illness compatible in its symptoms with acute coccidioidomycosis.

(2) *Cutaneous tests.* Coccidioidin injected intradermally in 0.1 cc. volume of two concentrations, 1/1000 and 1/100. The results are read at the end of 48 hours and recorded as positive if the area of induration and erythema is or exceeds 0.5 cm. in diameter. A reaction measuring 0.5 to 1.0 cm. in diameter is recorded as +, 1.0 to 2.0 cm. as ++, exceeding 2.0 cm. as +++, and extensive induration with vesiculation or necrosis as +++++. The test is highly specific and indicates coccidioidal infection past or present. A positive result from patients from whom a previous test made before the onset of the current illness had given a negative result is of special diagnostic value. A negative result usually excludes infection except in severe and overwhelming infections.

(3) *Culture and animal inoculation.* Culture from pus is usually easy but when other microorganisms are present as in the case of sputum it is advisable to use a selective medium such as the following:—

	Per cent.
Ammonium chloride	1.0
Tribasic potassium phosphate	0.8
Agar	2.0
Copper sulphate (add after autoclaving)	0.04

Inoculation into mice or guinea-pigs is desirable to establish the identity of the fungus isolated.

(4) *Tests of the patient's serum.* Precipitin and complement fixation tests with coccidioidin antigen are valuable in diagnosis and in prognosis. In the earlier stages of the disease the precipitin reaction is usually found stronger than the complement fixation test but it tends to diminish earlier in the stage of recovery. A diminishing precipitin reaction with a rising complement fixation titre is of bad prognosis and usually heralds dissemination of the disease. Focalization of the disease is associated with the disappearance of both reactions or the persistence of a feeble complement fixation reaction.

(5) *Examination of tissue.* Demonstration of the parasitic spherules in tissue removed at biopsy is frequently difficult and it is advisable to combine this examination with culture and inoculation into animals of the tissue material or if necessary of the culture obtained.

(6) *Examination of the blood.* There is no significant alteration in numbers or proportions of the leucocytes in the chronic stage of the disease. The sedimentation rate is an important guide to progress: it increases during the active stages of the disease and its fall to the normal several weeks or months after the febrile reaction has subsided is a good indication of recovery.

(7) *Radiography*. X-ray examination of the chest is of the greatest value in detecting the pulmonary lesions and especially the associated involvement of the bones.

The authors conclude with a discussion on treatment, from which it seems that the best course is rest, as complete as possible until the symptoms subside. The results from chemotherapy have been disappointing but immune-therapy using the blood from a recovered case seems worth further trials.

J. T. DUNCAN.

CALLAHAN W. P. Jr. Spontaneous Histoplasmosis occurring in a Dog. *Amer J Trop Med* 1944 Nov., v 24 No. 6 363-6 2 figs. [14 refs.]

DE MOXBREUN [this *Bulletin* 1940 v 37 533] was the first to diagnose naturally acquired histoplasmosis in the dog. TEUBINGER [this *Bulletin* 1944 v 41 774] described the second case and the present author adds the third. With this dog, as with the other two the source of the infection is not known but shortly before the onset of symptoms the animal had been boarded at kennels in St. Louis in which city three cases of histoplasmosis in man had previously been reported. The diagnosis was made from the examination of tissue sections three months after the animal's death so it was not possible to obtain a culture of the causative fungus. However excellent sections of spleen and mesenteric lymph node showing clearly the characteristic lesion of histoplasmosis place the diagnosis beyond question. The author refers to the earlier reports by SANGUINETTI (*Pathologica* 1922, v 14 483) and SHORTT (*Indian J Med. Res* 1923 v 10 908) of yeast-like bodies in the organs of mice and by LEVINE *et al* (*Cornell Veterinarian* 1938, v 28 249) of a similar kind of parasite in the organs of a ferret. From the descriptions given of the lesions and the associated microorganisms competent observers have concluded that these animals may have been suffering from infection by a species of *Histoplasma*. The probable existence of an animal reservoir of histoplasmosis must be considered.

J. T. DUNCAN.

TROPICAL OPHTHALMOLOGY

A REVIEW OF RECENT ARTICLES. XLV*

Trachoma.—The treatment of trachoma with special reference to local sulphonamide therapy is discussed by SOREBY¹. A series of 200 patients were treated in the White Oak Hospital and the Eastern Fever Hospital under ideal conditions for continuous observation, and allowed a certain amount of experimentation in treatment. Before the advent of the sulphonamides only three preparations (of a multitude suggested by the literature on the subject) were found useful: saturated solution of quinine bisulphate, mercury per chloride and Trachocid. Saturated solution of quinine contains about 2 per cent of the salt in solution. Mercuric chloride is generally used as a paint in 1-2 per cent. solution in glycerine. Trachocid is a proprietary preparation said to contain bee-venom, and manufactured by the State Serum Institute in Vienna. It is recommended for use by injection under the conjunctiva. Soreby's classifica-

*For the 44th of this Series see v 1 41 pp 1080-1082.

¹SOREBY A. The Treatment of Trachoma, with special reference to Local Sulphonamide Therapy. *Brit. J Ophthalmol.* 1945 Feb v 29 No. 2, 93-102.

cation of trachoma was based on therapeutic requirements. Stage I was moist active trachoma with sodden fornices and formation of follicles. Stage II represented a moist tarsal conjunctiva ideally without follicle formation and but little swelling of the fornix. Stage III stood for Stage II but with the conjunctiva no longer moist it was trachoma in the process of healing. Treatment aimed at the rapid conversion of Stage I into Stage II. The passage of Stage II to Stage III was a more prolonged process. The sulphonamides have proved to be valuable agents in trachoma therapy. They were at first used by oral administration and later by local application. The following procedures were carried out: (1) Full doses of sulphapyridine, sulphathiazole or sulphamerazine (the last being the best as it is least toxic) for 10 days. (2) Mechanical expression of the follicles and the contents of the fornix under local anaesthesia. This might have to be repeated after 7-14 days. (3) The conjunctival surface thus treated was painted immediately with saturated solution of quinine, repeated three times daily for 7-14 days. Two alternative methods of treatment are open:—(1) Painting the lids twice daily with glycerine solution of mercury perchloride $\frac{1}{4}$ -1 per cent. (in the case of children) or 1-2 per cent. (in adults); the paintings should be continued till the eye becomes dry. More recently better results have been obtained by (2) painting the lids with 30 per cent. sodium sulphacetamide solution ('Albucid') once daily and instilling sodium sulphacetamide ointment 6 per cent. three times daily. The eye rapidly becomes dry, all follicles disappear and the fornix looks almost normal. Stage III is characteristically a dry eye. In most cases nothing need be done though there is no harm in using $\frac{1}{4}$ per cent. copper sulphate or zinc sulphate drops. The continued use of sulphacetamide ointment is helpful. Pannus regresses with proper management of the conjunctival lesion. Massage of the upper third of the cornea with a small glass rod is a useful procedure. In more active corneal lesions atropine is indicated and a course of oral administration of some sulphonamide may be necessary. For dense pannus and active corneal lesions subconjunctival injections of 0.5 cc. of the mixed solution of Trachocid at 2 or 3 points in the circumference of the cornea were found helpful. If a corneal ulcer develops, carbolicising with 30 per cent. sulphacetamide solution may be carried out.

Sorsby points out that the application of the copper stick is a barbarous procedure and most ophthalmologists will agree that it has no place in the modern treatment of trachoma and should be discarded.

The author is strongly of opinion that sulphonamides are specific against the as yet unisolated trachoma virus and that expression with the local application of sulphacetamide can bring about a clinical cure of trachoma.

GILFORD² reports the treatment of four Russian patients suffering from trachoma with penicillin drops (16 000 units per cc.) given three-hourly in both eyes for three days. These cases showed well marked vascularization of the cornea and pannus. All four resolved rapidly under penicillin treatment. It still remains to be proved that it has a specific effect on the virus causing the disease or whether the effect is only transitory clearing up the secondary infection present in all these cases.

The investigation of trachoma and some observations on blindness in Cyprus are discussed by SHELLY³ who states that it is there a family and social disease more prevalent in the villages than the towns and practically non-existent in the mountain districts. He found that either the whole family was

*GILFORD, G. H. Treatment of Trachoma with Penicillin. [Correspondence.] *Brit Med J* 1945 Feb. 17 232-3.

²SHELLY, J. E. Investigation of Trachoma and some Observations on Blindness in Cyprus. *Acta Med Orientalia (Palestine & Near East Med J)* 1945 Jan. v 4 No 1 21-6.

penicillin, and stopped as soon as these became available. The author points out that if in this case it had been possible to start penicillin therapy early and in adequate dosage it is likely that rapid recovery would have ensued without complication. But the ultimate recovery suggests that even when a severe infection comes under treatment at a late stage penicillin is worth a trial.

E O'G KIRWAN

FAMILIARI P. Considerazioni clinico-sociali sulla diffusione del tracoma fra la popolazione indigena dell'Africa Orientale Italiana. [The Spread of Trachoma among the Natives of Italian East Africa.] *Boll. Soc. Ital. di Med. e Ig. Trop.* (Sez. Eritrea) 1944 v 3 No. 1 464-66. [55 refs.]

The clinical forms of trachoma and the social conditions amid which it prevails are much the same in Eritrea and Somaliland as elsewhere. The characteristics so far as they apply to Italian East Africa, are detailed and discussed by the author. Trachoma is endemic in the country but becomes epidemic in waves of shorter or longer duration and of greater or less intensity from time to time. ZAKATTIN examined 8 000 individuals with eye affections in Asmara and found 70 per cent. of them suffering from trachoma. PERGOLA in 1937 found 61.2 per cent. among 1,338 at the Regina Elena hospital and 68.3 per cent. the following year between 1939 and 1942 in the Ophthalmic Department of the hospital trachoma accounted for 46 per cent. of the patients and 44 per cent. of eye operations were for the alleviation of cicatricial effects of the disease. It is noted that there are two peculiar characteristics of the indigenous trachoma its benign onset and course and the gravity of relapses and complications. The disease is as usual, largely one attacking the poor and ill-nourished, while climate plays no small part—a relatively damp atmosphere near the sea, with prevailing north-east winds and the almost perpendicular rays of the sun near the equator.

Debilitating diseases also predispose in this area particularly malaria, ankylostomiasis and syphilis. The conditions amid which the people live are very unhygienic personal cleanliness is almost unknown, they hardly ever wash face or hands and they live in dirt more like animals and never give a thought to spread of disease and infection by contact. With such a people and in such circumstances to deal effectively with the disease is no light undertaking.

H Harold Scott

GILBERT W. Ergebnisse der Sulfonamidbehandlung bei Trachom und anderen Augenerkrankungen. [Results of Sulphonamide Treatment in Trachoma and other Diseases of the Eyes.] *Med. Klin.* 1943 Oct. 29 v 39 No 43/44 721-3.

This is a review article speaking in general terms and giving few if any particulars. The author starts by acknowledging the difficulty of assessing the results of treatment of trachoma because some cases recover without any treatment others have chronic sequelae and others again suffer from relapses. He does not express his own opinion, or give his own experiences, but quotes from the literature and the reports of others. Practically the only figures he gives are those from treatment with albucid [sulphacetamide] prontosil and eubasin [sulphapyridine]. Albucid has a twofold action—on the virus and on the trachomatous tissue. "Forty-eight per cent. of patients followed up could be regarded as cured [but this seems to refer to 23 cases only reported by ORENZ]. Of 145 cases of different stages of trachoma treated by GLOWATSKY half were given eubasin and half albucid 93 per cent. were clinically cured. Sulphonamides left a residue with scars (nebulae) and in this respect albucid presented a certain superiority" over eubasin [but no comparative figures are given].

The author concludes: Most observers look upon sulphonamide treatment of trachoma as a definite advance—it has raised the percentage of cures and cuts short the time needed for cure. Alhucid has proved to be the best but eleudron [sulphathiazole] eubasin cibazol [sulphathiazole] and other sulphonamides also proved serviceable [in the absence of details such a general statement does not convey much useful information]. Local treatment by ointment and subconjunctival injections are not of much benefit unless combined with internal administration—three tablets each of 0.5 gm. three times on the first day twice on the second and third days repeated if necessary after an interval of 3–4 days. Its beneficial action is shown by rapid retrogression of the inflammation, reduction of secretion and healing of the corneal complications.

Good reports have been made, says the author [in these general terms only] on the benefits of sulphonamide drugs in acute purulent affections of the lids and tear ducts in corneal ulcers especially *ulcus serpens* and in gonococcal infections of the newborn. As drawbacks to the use of these drugs transient myopia has been not infrequently observed, with spasm of accommodation, some swelling of the lens and slight rise of intraocular pressure. Spasm of the ciliary muscles does not alone explain the myopia—it is due in part to the changes in the lens. H. Harold Scott

HEYDEN G. Erfolge der Trachomtherapie [Results of Treatment of Trachoma.] *Deut. Militärarz.* 1944 Mar. v 9 No 3 135–7

We must not be surprised at reading in a German paper that trachoma prevails in 86 per cent of British India, in 80–90 per cent of Egypt, in 30–80 per cent of Russia, in 20 per cent of Japan and in only 1–4 per cent of Middle and Western European States and that the basic cause is bad conditions of hygiene. The lines of treatment are early eradication by application of silver nitrate or copper sulphate and, later, plastic operation. The author proceeds to remark on newer methods, mentioning the local use of chaulmoogra oil to the lids every two or three days which, he says, gives poor results; repeated application to the conjunctiva of dilute cyanide of mercury [the degree of dilution is not stated]; the local use of X rays (which causes considerable pain and moreover is usually ineffectual). Sulphonamide drugs as subconjunctival injections of 0.2 cc. of 5 per cent. protosil [how often the author does not say] together with its administration *per os* [dose not stated] brought about cure of 16 out of 53 cases in one month, in another 16 in two months, 7 in three months, 4 in four months and 2 in six months. [A report based on only 53 cases is not very convincing.] H. Harold Scott

FILATOV V. P. Tissue Therapy in Ophthalmology. *Amer. Rev. Soviet Med.* 1944 Oct. v 2 No 1 53–68 46 figs. (44 on 4 pls.)

The author maintains that when animal and plant tissues are isolated and stored under certain conditions substances accumulate in them which stimulate metabolic processes. These substances have been named biogenic stimulators. Their chemical nature is unknown. When tissues rich in biogenic stimulators are introduced into a diseased organism by transplantation or by injection of extracts the regenerative powers of the treated organism are increased and the pathological processes are suppressed.

Tissue, usually skin or cornea, may be removed aseptically within 10 hours of death from the cadavers of persons who have died of non-infectious diseases or from trauma and be transferred to a sterile bottle and stored at 2–4°C for seven days. Spirochaetal infection if present totally disappears in this time. Autoplastic material (usually skin) may be obtained from the living subject

and stored in the same way while homoplastic material (skin or placenta) may also be employed. Placenta is usually made use of in the form of a sterile aqueous extract. Animal material, such as skin, testis etc. from rabbits sheep and calves, the aqueous humour from cattle eyes, and spinal fluid, has also been used. "Biogenic stimulators" are reported to be present in cod liver oil and aloe leaves.

For administration, skin, preserved by refrigeration, is implanted subcutaneously and kept in place by interrupted sutures. Healthy granulation tissue forms at the site of the transplant. Therapeutic grafting of preserved cornea is carried out like a partial lamellar transplantation. Placenta and other tissues which have been refrigerated for seven days may be implanted into pockets made by incising into the subcutaneous tissue or into the subconjunctival tissue. Fluids (aqueous humour blood, spinal fluid or aqueous extracts of preserved tissues or aloe leaves) are injected subcutaneously or subconjunctivally.

This treatment has been used successfully in cases of lupus vulgaris tuberculous ulcers lupus erythematosus, gummata, and cutaneous leishmaniasis etc., but the author gives greatest attention to ophthalmological conditions. He has used this method of therapy in interstitial keratitis, in tuberculosis of the cornea (with successful results in 21 out of 25 cases) in keratitis rosacea (five cases) in trachomatous pannus (300 cases) in uveitis, in retinitis pigmentosa (112 cases) in myopic choroidoretinitis (250 cases) in atrophy of the optic nerve (or over 100 cases) and in glaucoma (60 cases).

The results are reported to have been very satisfactory particularly in optic atrophy retinitis pigmentosa, and keratocoma. J A Davidson.

HEAT STROKE AND ALLIED CONDITIONS.

SIMPSON H. M. D. Effects of Heat in Iraq *J Roy Army Med Corps* 1945 Jan., v 84 No. 1 1-8.

A description is given of cases of effects of heat seen during three summers in the plains of Iraq. The cases are divided into four types —

- (i) *Acute heat stroke*—This conformed to the usual description. The chief features were loss of consciousness, and a rectal temperature of more than 106°F. No specific mention is made of inability to sweat.
- (ii) *Heat exhaustion*.—These patients were dehydrated, often with a low blood-pressure or pulse-pressure. The urinary chlorides were reduced or absent. The cause was therefore considered to be salt-deficiency.
- (iii) *Subacute effects of heat*.—These patients had a moderate pyrexia—up to 103 or 104°F.—which might continue for as long as two weeks, with vomiting, muscular twitchings, convulsions, or mental changes, varying from slight disorientation to violent mania. The first sign of trouble was often the occurrence of a fit or a change in behaviour. Some patients of this type were first admitted as mental cases.
- (iv) *Heat pyrexia or short fever*.—These patients had a temperature for a few days and then recovered without indication of the cause. The author argues that the cause was heat—the cases showed none of the features of malaria, dengue or sandfly fever. The incidence depended on the weather—more patients were admitted on the hot windless days than on the less hot days.

Diagnosis and treatment of all cases are discussed on standard lines. In connexion with prognosis some points of great practical importance are brought out, which may be given in full —

(1) Mental changes whatever the temperature constitute a most dangerous sign and demand vigorous treatment.

(2) Vomiting is a dangerous sign except in patients who are beginning to recover from heat-stroke. In these provided it lasts only a short time it is a sign of improvement.

(3) A patient with heat-stroke should never be regarded as past hope until he is dead. There is no other condition in which a patient can look so ill and yet recover.

(4) It may be more dangerous for a man to have severe subacute effects of heat than it is for him to have heat-stroke. The reason for this is that heat stroke is an obvious emergency and receives vigorous treatment whereas subacute effects of heat may not. Also the subacute case in the later stages is more resistant to treatment than acute heat-stroke.

[The classification of types of effects of heat that is given here is in close agreement with that proposed by other recent workers (see LADELL *et al* this *Bulletin* 1945 v 42, 143). In spite of much that has been published on heat effects the nature and cause of the subacute type remains singularly obscure. The reviewer working in Southern Iraq in 1943 did not see a single patient of the subacute type among some 200 cases of effects of heat that occurred in the area. Cases had however been fairly numerous in 1942 which was hotter than 1943. It is not clear whether these patients were dehydrated and salt deficient whether there was any disturbance of sweating nor even whether they represented a distinct type of effects of heat or whether they developed from some other type through lack of adequate treatment. There is little in the literature to add to what Major Shepherd has said.

The symptomatology is protean, and the prognosis bad. For this first reason more information is urgently needed. This should include —

- (i) condition of the skin with regard to sweating scaling and prickly heat
- (ii) presence or absence of signs of dehydration
- (iii) blood pressure both lying down and standing up
- (iv) urinary volume specific gravity and chloride content
- (v) plasma chloride and blood urea values

J. Waterlow

MARSH F. Animal Life in Deserts. [Correspondence] *Lancet* 1945 Mar 3 289

The writer of this letter whose work on heat stroke is well known, refers to the paper by LADELL, WATERLOW and HUDSON [this *Bulletin* 1945 v 42 143]. He states that loss of body weight in hot weather is not a feature of well acclimatized persons they may in fact show increase in weight by developing an oedematous hump to keep them going between drinks of water.

A striking feature of heat exhaustion is the stuporose mental reaction which however clears up after two or three days rest in bed. A cool room is essential for effective treatment. Marsh states that the natural inclinations are no guide to the amount of water needed in these desert conditions it is necessary for a man to drink 12-30 pints of water a day with equivalent amounts of salt but he may not actually feel the need for such quantities. Moreover these large amounts may lead to acute dyspepsia but there is no other route for water absorption.

Anoxia has been associated with therapeutic hyperthermia, and Marsh has given oxygen with success in cases of heat exhaustion. He remarks on the need for careful selection of men for service in the tropics and on the importance

of careful acclimatization before exposure to the most severe heat. Air conditioning of quarters and hospitals is needed. An attack of sandfly fever or other fever or even temporary dehydration may stop sweating by some central action on the hypothalamus.

Charles Wilcocks

BLACK, D. A. K. Dehydration. *Lancet* 1945 Mar 10 298-300. [10 refs.]

After a brief discussion of the normal intake output and distribution of water in man two different types of dehydration are considered—the one is due to water deprivation the other secondary to salt deficiency.

Water Deficiency—Experimental subjects on a dry diet can go without water for three or four days [but only in temperate climates] without becoming really ill. After an initial rapid drop the weight falls slowly blood urea rises plasma sodium and chloride also rise but there is no haemoconcentration as about two-thirds of the water lost is intracellular in origin. The urine volume is low (about 500 cc. per day) but this is not due to renal failure—the urine has a high specific gravity (above 1000) and is concentrated. Diureses in response to salt or to urea are obtainable (some workers believe that a urine volume of 500 cc. or more per day is due to excessive protein catabolism when protein intake and breakdown have been cut to a minimum much lower urine volumes have been obtained during water deprivation).

Salt Deficiency—In contrast to water deprivation salt deficiency is associated with marked apathy and exhaustion and with painful cramps. Nearly all the fluid lost is extracellular and there is a fall in plasma sodium and chloride. The extracellular fluid loss is shown by haemoconcentration, and it results in circulatory failure. The urine volumes are not so low as in water deprivation and the urine is more dilute.

In practice dehydration is usually mixed—the treatment required depends on the factor predominating, which may be diagnosed from the subject's history and clinical condition and from laboratory investigations. If the fluid loss has been mainly from the skin and lungs water deprivation predominates if the dehydration is due to vomiting or diarrhoea, there is considerable salt loss. Clinically circulatory failure and muscle cramps are indications of severe salt deficiency. Laboratory investigations should include examination of the urine for chloride of the blood for haemoconcentration and, if possible estimation should be made of plasma chloride and sodium. For water deficiency water or 5 per cent. glucose should be given for salt deficiency normal saline and in mixed cases varying proportions of half normal (0.45 per cent.) and normal saline as the condition of the patient indicates. Hypertonic saline is only rarely required. It is important that the water and salt requirements of the patient should be reassessed daily the various investigations being repeated as often as possible.

W. S. S. Ladell.

TROPICAL ULCER.

MIMA, H. Sulphonamides and Tropical Ulcers. [Memoranda.] *Brit. Med. J.* 1945 Mar 17 369.

The author has treated tropical ulcers successfully as follows—Paint the ulcer with 2½ per cent. tincture of iodine special care being taken to see that it reaches well under the enveloping edges. Allow it to dry then cover it with a layer of powder made up of equal parts of sulphathiazide and magnesium sulphate. Repeat treatment daily until cured.

Notes of three cases are given—an old much-treated ulcer 2 inches wide and half an inch deep in a girl aged 11 years healed in eight days—an ulcer 4 inches long 2 inches wide and 1 inch deep in a woman aged 40 healed in two weeks—a sloughing and gangrenous area on the forearm 4 inches long which had developed after a comminuted fracture healed in two months.

No bad effects of the drug have been observed. The author states emphatically that aqueous antiseptic solutions should never be used to treat tropical ulcers.

J F Corson.

HAMM W G & QUARY G. Penicillin Therapy in Phagedenic Ulcer (Tropical Sloughing Phagedena). Report of Eighteen Cases. *U.S. Nav Med Bull* 1944 Nov v 43 No 5 831-7

Penicillin was used as a local dressing in 18 cases of tropical ulcer—at first intramuscular injections were tried but the patients who were all natives [race or country not mentioned] objected strongly and it was abandoned though good effects were observed.

The ulcer was cleaned and gauze soaked in a saline solution of penicillin containing 2,500 units per cc. was applied. Although dressings could be changed once a day only owing to the limited supply of penicillin and although the patients persisted in walking as soon as the pain had ceased strikingly good results were obtained. The treatment was continued for 2 or 3 days after the ulcer had become clinically clean and the fusiform bacilli and spirilla had disappeared wet saline dressings were then used. The penicillin dressings caused no pain and no irritation of the skin nor did they unfavourably affect subsequent skin grafting. Notes of the 18 cases are given and show excellent results complete healing having taken place in 3 or 4 weeks in most of the cases some without skin grafts.

The authors conclude that it is perhaps the most efficacious of all forms of therapy that have been used in the treatment of phagedenic ulcer.

J F Corson

MISCELLANEOUS DISEASES

FETTERMAN G H MORAN T J & HESS W R. The Cold Agglutination Test I. Studies on Naval Hospital Patients. II. Studies on Natives in Yaws-Endemic Area. *U.S. Nav Med Bull* 1944 Dec. v 43 No 6 1123-38. [Summary appears also in *Bulletin of Hygiene*]

Cold agglutinins in high titre have been observed to occur regularly only in the following diseases—primary atypical pneumonia of unknown aetiology [*Bulletin of Hygiene* 1943 v 18 818 & 897] African trypano omiasis (KANTHACK, DURHAM and BLANDFORD *Proc Roy Soc.* 1898 v 64 100 *Sleeping Sickness Bulletin* 1908 v 1 60 1910 v 2, 331 and 400 1911 v 3 53) paroxysmal haemoglobinuria (STATS and WASSERMAN *Medicine* 1943 v 22 383) and mumps (TURNER NISNEWITZ JACKSON and BERNET *Lancet* 1943 June 19 765) DAMESHEK [*Bulletin of Hygiene* 1944 v 19 180] reported their occurrence in haemolytic anaemia after sulphonamide therapy Cold agglutination [autoagglutination] has also been observed to occur irregularly in many other conditions (STATS and WASSERMAN *loc cit*)

The authors carried out tests on human blood sera at a Naval hospital laboratory in a South Pacific island—the patients included many members of the Naval personnel suffering from various diseases and also some natives in the island. They used the technique of HORSTMANN and TATLOCK [*Bulletin of Hygiene*,

1943 v 18 897] the readings being made with the naked eye. The diseases of the Naval hospital patients included lobar and broncho-pneumonia, bronchitis, bronchial asthma and related conditions, clinical pulmonary tuberculosis, many contagious and infectious diseases, in particular malaria, syphilis and mumps with orchitis. Some healthy controls were also examined.

Among the respiratory diseases primary atypical pneumonia alone showed titres higher than 1:16 and among the 158 patients with other diseases—which included malaria, dengue, filariasis, infective jaundice, syphilis, gonorrhoea (treated with sulphonamide), mumps and several other diseases, only one, a case of mumps with orchitis (titre 1:32) had a titre above 1:16. In some cases significant titres were found during the first week of the disease [see HEISTEELMAN & SELIGMAN *Bulletin of Hygiene* 1945 v 20 244]. The 14 healthy controls gave negative results except one who had a titre of 1:8.

The examination of the sera of natives of a yaws-endemic area gave interesting results—they are shown in the following Table—

TABLE 3.—Cold agglutinins in native groups

Race and condition	Number of individuals	Cold agglutinins	
		1:16 or less	1:32 or less
Melanesians	68	38—(24)	48—(32)
Lepers	52	19—(10)	33—(18)
Non-lepers	34	19—(14)	15—(14)
Malayans and Caucasians	35	30—(2)	5—(2)
Lepers	20	17—(1)	3—(2)
Non-lepers	15	13—(1)	2—(0)

Note.—Figures in parentheses indicate number of individuals having positive Kahn reactions.

The authors concluded that leprosy was not the underlying factor: the healthy non-leprosy Melanesians had more high titres than the non-leprosy Malaysians and Caucasians, but they also had more positive Kahn reactions, probably due to yaws, which is endemic. The positive Kahn results, however, were about evenly distributed among persons with high and low cold agglutinin titres, and none of the Kahn-positive cases of syphilis among Service personnel had a high titre in the cold agglutinin test. The authors think that yaws may be a factor, though they mention the possibility that there may be some unrecognized factor or disease. A further study of yaws could not be made.

They concluded that a titre of 1:32 or over in Service personnel, was strong evidence for the diagnosis of atypical pneumonia.

J. F. Corson.

HERTEL, H. W. Über "russisches Kopfschmerzfiel" im Westen. ["Russian Headache Fever" in the West.] *Deut. med. Woch.* 1944 July 7 v 70 No. 27/28, 390-91.

The author regards three cases of short fever seen by him in western Europe as belonging to the same type as the "Russian headache fever" described by SCHULTZ and BROGLIE [see this *Bulletin* 1944 v 41 127] and the fever described by SYLLA (*ibid.* 1281).

There were some points of clinical difference, but these are regarded as falling within the limits of variability of a fever of this kind.

The three cases occurred quite independently of each other the onset in the case that is fully described was on December 22nd, 1943 [In the two fevers mentioned above the cases occurred in August September and October and the disease disappeared in the cold season]

The author states that lice and other parasites could be excluded as transmitting vectors and that there was no indication to show the mode of transmission. He regards the disease as a meningoencephalitis probably caused by a virus. No bacteriological or serological investigation was considered necessary because the clinical features did not suggest typhoid or typhus fever.

[No reference is made to the possibility that the disease might have been caused by a strain of influenza virus. The clinical description seems to be compatible with this hypothesis.]

John W D Megaw

KNOTT J I "Filarial Abscesses. [Correspondence.] *Trans Roy Soc Trop Med & Hyg* 1944 Dec. v 38 No 3 235

The author treated intramuscular abscesses in natives of the Cook Islands by aspiration using an intravenous transfusion needle. Early abscesses were usually cured even if only 1 cc. of pus was withdrawn large abscesses required two or more daily aspirations. In many cases a patient who was carried to the hospital could walk home after the aspiration. Smears of the pus showed leucocytes packed with staphylococci. Although most of the people had filariasis no connexion between this and the abscesses was found. Treatment of intramuscular abscesses with sulphonamides was ineffective J F Corson

CLEARKE P A. Tropical Eosinophilia or Loeffler's Syndrome *Caribbean Med J* 1944 v 6 No 5 252-6

A report of a case in British Guiana.

ANDERSON T F BRIGGS F H H. & McNAUGHTON F. Poisoning with Datura. *East African Med J* 1944 Dec. v 21 No 12, 355-61 1 fig

During a period of 10 months October 1943 to August 1944 cases of food poisoning totalling 1 524 occurred among recruits and African troops in Uganda. There were no fatalities among them and no Europeans reported sick from this cause. All those attacked had been supplied with flour issued from two cook houses. The chief symptom (in some the only symptom) was dryness of the mouth and throat others suffered from visual hallucinations loss of memory mental excitation even to mania mydriasis was not common. The attacks were on the whole mild and recovery took place within 24 hours.

Some toxic component of the flour was suspected first *Lolium temulentum* [which however is usually associated with vertigo staggering gait tremors burning sensations in the throat and prostration] then Cassava as the Bitter Cassava contains a cyanogenetic principle but the actual cause was found to be admixture of the seeds of Datura. The fact that only Africans no Europeans were affected is explained by the wheat intended for flour being cleaned and any contaminating Datura removed by the millers prior to grinding, whereas wheatmeal supplied to the Africans is ground by small millers who either do not know or have no facilities for separating the adulterating Datura seeds [See also this *Bulletin* 1938 v 35 837 for a similar occurrence in Tanganyika Territory in 1938] [The seeds of Datura closely resemble mustard seed and are [or used to be] commonly added to the latter by thieves in India and mixed with the food of their intended victims to stupefy them while they robbed them. The victims on recovery usually retained no consciousness of their attack.]

H Harold Scott

RAYMOND W D A Short Note on Human Datura Poisoning in Tanganyika
East African Med J 1944 Dec. v 21 No 12, 362-4

Dr Raymond contributes an interesting note on Datura and poisoning by its seeds. The fruit he states also contains the toxic alkaloids hyoscyne, hyoscyamine and atropine especially the first, but only about one-fifth the amount present in the seeds. These seeds may be present accidentally in meal, as in the outbreak reported above and Raymond mentions the case of a European under his own observation who was poisoned by Datura-contaminated meal. The secret drug known as Lukuma added to native food (pombe) by would-be robbers is Datura. It is administered for producing insensibility to facilitate theft and not for homicidal purposes but those who employ it do not always stop to measure dosage and fatal cases sometimes occur. In meal the contamination is accidental and consequently unevenly spread, and the author shows that some samples contained 0.02 mgm. per 100 gm. others more than eight times this amount. Prolonged cooking in water destroys fully half the toxic alkaloids.

H Harold Scott.

WRIGHT F J A Note on Poisoning by *Datura stramonium* in Civilian Practice.
East African Med. J 1944 Dec. v 21 No. 12, 365-7

The author has seen nine cases of Datura poisoning in the last three years three of the patients were Indians who may have taken the seeds purposely. As the patient may be comatose when first seen the diagnosis is not easy and other causes of coma must be excluded, meningitis, cerebral malaria, cerebral haemorrhage, diabetes etc. but if these are excluded and if the stomach contents can be examined the seeds or fragments of them will be found. Apomorphine in most cases (if the coma is not very deep) will result in vomiting, but if there is deep coma the vomiting centre is depressed and cannot be stimulated.

The Editor of the *East African Medical Journal* adds an interesting footnote telling how children may be poisoned by "sucking the honey out of the nectaries at the base of Datura flowers" and chickens by being given Kenya chickweed heavily contaminated with the seeds. He remarks also on the varying susceptibility of different animals to Datura: rabbits are almost insusceptible and can eat 100 gm. a day without showing any symptoms; cats are also tolerant but less so than rabbits; while cattle and horses are less tolerant than are sheep.

H Harold Scott.

MARIANI TOSATTI G Avvelenamento da Datura Stramonium (Quattro casi)
 (Four Cases of Poisoning by *Datura stramonium*) *Boll. Soc. Ital. di Med. e Ig. Trop.* (Soc. Eritrea) 1944 v 4 No 2, 295-303. English summary
 (3 lines)

All four patients were children: a girl aged 10 and three boys aged 3, 5 and 8 years, observed by the author in Asmara. They had wandered unsupervised in a garden and all presented a similar train of symptoms—flushed face, dilated pupils, dry throat, laughing and crying and giving signs of hallucinations; the oldest child had a staggering gait and kept falling into brief snatches of sleep and then waking and calling for something to drink. All the children recovered. The rest of the paper is taken up with general remarks on Datura.

H Harold Scott

GENERAL ENTOMOLOGY

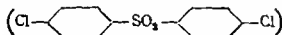
DAVID W. A. L. *Insecticidal Sprays and Flying Insects.* [Correspondence.]
Nature 1945 Feb 17 204 3 figs

Insecticidal mists have very little action on flies or mosquitoes at rest. In order to be effective the droplets of spray must impact upon the insect. This may perhaps result from the movement of the droplets imparted by the spray gun but the active movements of the insect during flight are much more important in bringing about impaction. Experiments with *Aedes* and *Musca* here described prove that by far the greatest number of droplets impact upon the wings. The wings are then cleaned with the legs and in this process the insecticide is brought into contact with the feet which are known to be one of the most permeable regions. In *Musca* much of the insecticide may be removed from the fore-feet by the proboscis and swallowed and may thus perhaps act as a stomach poison. If the wings are removed just after exposure to an oil spray mist the kill may be reduced by about 50 per cent in comparison with a group with wings intact. Clearly a substance such as pyrethrum, which excites the insects to flight is a desirable constituent in fly and mosquito sprays.

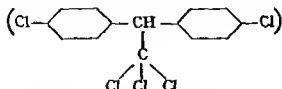
V B Wigglesworth

LÄNGER P MARTIN H & MÜLLER, P Ueber Konstitution und toxische Wirkung von natürlichen und neuen synthetischen insekten-tötenden Stoffen. [Constitution and Toxicity of Natural and of New Synthetic Insecticides.] Reprinted from *Helvetica Chimica Acta* 1944 v 27 No 4 892-928 12 figs. (10 on 4 pls) [Summary appears also in *Bulletin of Hygiene*]

In this interesting lecture some account is given of the search for new insecticides carried on by the Swiss firm of J. R. Geigy A.G. in Basel over a period of more than 10 years which culminated in the discovery of the insecticidal properties of 4,4'-Dichlorodiphenyltrichloromethylmethane generally known as DDT. The original purpose was to find a stomach poison for clothes moths with which textiles could be impregnated. One of the most promising materials proved to be 4,4'-Dichlorodiphenylsulphone

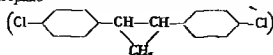


There was in fact much evidence that *pp'* halogenated compounds of this general type were highly insecticidal and it appears to have been a deliberate search among other compounds of that structure which led to the testing of DDT



DDT is a nerve poison which is toxic to insects in exceedingly minute doses. It is lipid-soluble and it is to this property that the authors attribute its efficiency as a contact insecticide its entry into the insect cuticle being favoured by the lipid material in the epicuticle. They conclude that the specific toxic properties reside in the two linked benzene rings chlorinated in the *pp'* position the lipid solubility being conferred by the chloroform residue which links the two benzene rings together. There is evidence that the more

the substance used in the place of the chloroform is lipid-soluble the more toxic is the compound, the most effective being that derived from another narcotic cyclopropane



I. B. Wigglesworth.

MOOSER, H. Die Bedeutung des Neocid Geigy für die Verhütung und Bekämpfung der durch Insekten übertragenen Krankheiten. [The Importance of "Neocid" (Geigy) for the Prevention and Control of Insect-borne Diseases.] *Schweiz med Woch.* 1944 Sept. 9 v 74 No. 36 947

This paper gives a brief summary of the facts recorded in full by LÄNGER, MARTIN and MÜLLER [above] and then surveys the applications of DDT in human hygiene ["Neocid" is the insect powder containing 5 per cent. of DDT patented by the Geigy firm for use against insects affecting man]. The powder has been highly successful for delousing. It is however somewhat slow in action, 12-48 hours being required before all lice are killed. A lasting action on clothing can be obtained by impregnating with a 0.2 per cent. aqueous emulsion of "Neocid TA." If not washed, such clothing remains active in killing lice for 1-3 months. Heavy impregnations of clothing remain effective after washing, but the method of washing greatly influences the degree of persistence and the author recommends a reimpregnation after each wash. Head lice are likewise killed by the emulsion but after treatment of the head with a 0.1 per cent. emulsion there is almost no insecticidal action persisting beyond 36 hours.

DDT applied to surfaces of walls etc. is highly toxic to flies which settle thereon. It is equally toxic to *Anopheles* and *Culex* mosquitoes and ROSE (among many other workers) has claimed that its application in this way will go far to control malaria in rural areas. Fleas are very susceptible to DDT and their larvae even more so. It is very useful for controlling fleas in animal houses and may prove invaluable in combating bubonic plague. Treatment of dwellings with Neocid dust will keep them free from bed-bugs for months.

V. B. Wigglesworth.

DOMENJOS, R. Experimentelle Erfahrungen mit einem neuen Insektizid (Neocid-Geigy) ein Beitrag zur Theorie der Kontaktgiftwirkung. [Experimental Studies on a New Insecticide, "Neocid" (Geigy) a Contribution to the Theory of the Action of Contact Poisons.] *Schweiz med Woch.* 1944 Sept. 9 v 74 No. 36 952, 1 chart. [10 refs.]

The author uses the name GNB (Gesarol Neocid-Basis) for the active principle in the insecticidal preparations "Gesarol" and "Neocid" produced by J. G. Geigy A.G., Basel, and commonly known as DDT. The most important general properties of this substance are its marked lipid solubility, its insolubility in water, and its almost complete lack of volatility.

Its action on the human louse has been studied in detail. Fabrics impregnated with solutions containing as little as 0.00001 per cent. DDT are still slowly toxic to lice. Even higher concentrations (0.01 per cent.) require a period of 24-30 hours to kill all the lice, but contact with the material for only one hour leads to a very high subsequent mortality. The affected insects first become excessively active and later incoordinated, with tremors, once these symptoms appear they never recover.

In mammals DDT also acts as a nerve poison. It causes no local irritation when applied to the skin or conjunctiva of man or animals. When given by mouth to animals as an emulsion in gum arabic the L.D.50 in gm./kilo was

mouse 1.6 rat 0.5 guineapig 2.0 rabbit 0.275 Administered in olive oil it was far more toxic mouse 0.175 rat 0.28. The poisoned animals showed hypersensitivity tremors and in the later stages epileptiform spasms with opisthotonus. There was no sign of any cumulative action mice and rats receiving 50 mgm per kilo of food material for 70 days showed no ill effects. Applied to the skin as an emulsion in gum arabic the L.D.₅₀ for the rat is given as about 1 000 gm./kilo but it is much more toxic when dissolved in olive oil mouse and rat 0.25-0.5 gm./kilo. It is concluded that the 5 per cent. preparations as marketed are practically non-toxic to mammals.

The remarkable toxicity of DDT to insects is attributed on the one hand to the lipoids in the cuticle which favour its entry through the integument and on the other to the existence in insects of a peripheral nervous system containing ganglion cells which lies immediately below the cuticle and is responsible for regulating muscle tonus.

V B Wigglesworth

MANDEKOS A. Toxische Wirkung von Neocid auf Larven Puppen und Imagines von *Anopheles* und *Culex*. [Toxicity of Neocid to Larvae, Pupae and Adults of *Anopheles* and *Culex*] *Deutsch. Tropenmed. Ztschr.* 1944 Feb-Mar v 48, No 3-8 84-8.

Because of the shortage of Paris Green which is not in any case completely satisfactory for the control of *Anopheles superpictus* in running water experiments were carried out with Neocid and with calcium arsenite. Neocid is a proprietary product containing 5 per cent. 2,2 bis (para-chlor phenyl) 1,1,1 trichlorethane (DDT).

The experiments were carried out during June-September 1949 when the prevailing temperature was usually between 28° and 30°C. Neocid was shown to kill culicines and anopheline adults in 3½ hours while the first symptoms of tremors and paralysis were apparent in 15 minutes. Larvae were killed in 3½-5 hours but pupae survived for 29 hours. The effect on the eggs of *A. superpictus* is uncertain.

Suspensions of 0.1 to 1.0 per cent. Neocid in water killed all stages of anopheline and culicine larvae in 3-10 hours according to the concentration used. In natural breeding places where conditions were such that Paris green and calcium arsenate gave unsatisfactory results Neocid applied as a 0.35 per cent suspension in water to give 0.035 gm. of the pure substance per square metre left only about 0.2 per cent. of the larvae alive.

The action of Neocid on adult mosquitoes was clearly shown by experiments in cowsheds where the application of Neocid in water suspension at the rate of 1 gm. per square metre (i.e. 0.05 gm. pure DDT) gave complete kills of anophelines for a month. Little or no advantage resulted from adding a small quantity of oil to the spray.

When natural breeding places are being sprayed with Neocid water suspensions the effectiveness of the treatment is increased by the presence of oil in the mixture. Under these circumstances the presence of oil is advantageous since it serves to distribute the Neocid much further over the water surface than occurs with plain water suspensions. Neocid at 0.15 gm. per square metre applied as a 0.2 per cent suspension was satisfactory in standing water but with stronger currents the concentration must be increased to 0.4-0.55 per cent. and the deposit to 0.8 gm. per square metre.

It is pointed out that ingestion or penetration of Neocid into the respiratory system of the larva is not a necessary preliminary to effective action as it is in the case of other larvicides. [It seems possible, however that the greater resistance of the pupae could be accounted for by the fact that they do not feed and so avoid ingesting the poison.]

Calcium arsenate at 3-5 per cent. in road dust was about equally efficient as 1 per cent. Paris green in a similar medium and might be used to replace the latter as a practical larvicide.

W A L. David

MULHENS K Ueber bisher nicht bekannte insektizide Eigenschaften der Baumwollsmilch (*Euphorbia dendroidea* L.) [A New Insecticide from *Euphorbia dendroidea*] *Deut. Tropenmed. Ztschr* 1944, Feb.-Mar. v 48 No. 3/3 79-84

The insecticidal properties of *Euphorbia dendroidea* were examined because it was reported to be used as a fish poison in Crete.

The plant is found growing in dry sheltered, stony places on Crete and the Greek mainland. It remains green despite the low rainfall and is eaten by animals. It reaches commonly 50 cm. in height and 80 cm. in circumference, with a total fresh weight between 500-2,000 gm. The toxic action was confirmed on *Gambusia*.

It was found that a drop of the milky sap placed on the back of ants and bugs killed the insects in a few minutes. A 1:100 dilution of the sap also killed bugs. Separate aqueous extracts were prepared of the stems, leaves and roots. The stems appeared to give a slightly less effective product but with extracts equivalent to 1.0 gm. of dry plant per 100 cc. of water kills of bugs amounting to 80-100 per cent. were obtained within a few minutes. An extract containing 2.5 gm. of dried leaf per 100 cc. stupefied *Ulex domestica*, but the insects recovered. When 1 cc. of a 5 gm./100 cc. leaf extract was atomized into a 500 cc. flask, the exposed house flies were invariably killed. *Culex* spp. and *Phlebotomus* spp. were killed by more dilute solutions. Experiments with dust showed that 0.5 gm. powdered leaf in a 500 cc. flask killed houseflies within 4-6 hours and *Phlebotomus* spp. in a much shorter period. Corresponding exposures were not effective against bugs.

Effective sprays were also obtained when the leaves were extracted with acetone and the resulting solution diluted with water. Solutions containing the equivalent of about 1.0 per cent. dry leaf powder were completely effective against house flies and bugs under the testing condition employed. The following formula is recommended for practical use. Extract 50 gm. of leaves for three days with 1 litre of water at 55°C., and to this add 0.5 litre of a 1 per cent. aqueous soap solution.

It appears that the extracts prepared from fresh and dried material are almost non-toxic to warm blooded animals.

W A L. David.

DOVE, W. E. Insect Repellents. *Soap* New York, 1945 Jan. v 21 No. 1 121 & 121B

This article gives a semi-popular account of the large amount of work that has been done in America in the search for synthetic repellents which will not be injurious when applied to the human skin. More than 4,000 compounds have been tested. Three have proved satisfactory from the standpoint of repellency (they will give complete protection in cage experiments [i.e. no single bite is received] for 120 minutes against *Anopheles quadrimaculatus* and 180 minutes against *Aedes aegypti*) and from the standpoint of toxicity. These are dimethyl phthalate, "Indalone" [*n*-butyl methyl oxido oxalate] and Rutgers 612 [2-ethylhexano diol-1,3]. Since these substances vary in effectiveness against different biting insects it has been found advantageous to mix them in the proportion of 6:2:2. This is helpful also from the point of view of supply. This mixture is much more effective than the essential oils which have been in use in the past.

F B Wigglesworth.

HOLDEN J. R. & FINDLAY G. M. Pyrethrum as a Tsetse Fly Repellent Human Experiments. *Trans Roy Soc Trop Med & Hyg* 1944 Dec v 38 No 3 199-204

Anti mosquito cream Mark II a vanishing-cream containing an unspecified quantity of pyrethrum was found to provide protection to man against the bites of *Glossina palpalis* up to at least six hours after application provided excessive sweating did not occur. The same cream also gives a considerable degree of protection against the bites of *Culicoides* sp. V. B. Wigglesworth

- i. FARNER D. S. & BOHART R. M. A Preliminary Revision of the *scutellaris* Group of the Genus *Aedes*. *U.S. Nav Med Bull* 1945 Jan. v 44 No 1 37-53 4 figs & 1 map [30 refs.]
- ii. — A New Species of *Aedes* from the Caroline Islands. *Proc Biol Soc Washington* 1945 v 58 59-62

i. In this paper certain forms previously regarded as varieties or sub-species of the mosquito *Aedes* (*Stegomyia*) *scutellaris* (Walker) often called *variegatus* (Doleschall) in the literature, are raised to specific rank and considered with other recently described closely related species. Geographical distributions are given, with a useful tabular statement for making identifications. Adult mosquitoes alone are considered.

Aedes (*Stegomyia*) *pseudoscutellaris* (Theobald) (= *variegatus* var *pseudoscutellaris* (Theobald) of Edwards 1926 and others = *scutellaris* var *pseudoscutellaris* (Theobald) of Edwards, 1932 and others) from Fiji, Samoa, Wallis, Ellice Islands, Cook Islands, Society Islands, Tuamotu, Marquesas Islands.

Aedes (*Stegomyia*) *tongae* Edwards (= *variegatus* var *tongae* Edwards 1926 and others = *scutellaris* var *tongae* Edwards 1932 and others) from Tonga Islands, Sikiana, Solomon Islands (probably an introduction to the latter see Buxton and Hopkins 1925 *London School Hyg & Trop Med Mem Ser* no 2 103).

Aedes (*Stegomyia*) *horrescens* Edwards (= *scutellaris* var *horrescens* Edwards 1935) from Tavuni, Fiji.

Aedes (*Stegomyia*) *pernotatus* Farner and Bohart from Espiritu Santo and Efate, New Hebrides.

Aedes (*Stegomyia*) *hebrideus* Edwards (= *variegatus* var *hebrideus* Edwards 1926 and others = *scutellaris* var *hebrideus* Edwards 1932 and others) from New Hebrides, Eastern New Guinea.

Aedes (*Stegomyia*) *quasiscutellaris* Farner and Bohart (= *variegatus* (Doleschall) of Edwards 1926 and others = *scutellaris* (Walker) of Edwards 1932 and others from Solomon Islands). Farner and Bohart (1944 *Proc. Biol. Soc. Washington* 57: 120) in proposing the new name *quasiscutellaris* have pointed out that the form which Edwards regarded as *variegatus* is not found in New Guinea and has in fact a restricted distribution which probably excludes the type locality of *variegatus* (Amboina) and of *scutellaris* (Aru Islands). They therefore hold that it is a new species. They have not attempted to recognize either *variegatus* or *scutellaris* since the type localities are outside the region they have under consideration. The name does not therefore necessarily replace either *variegatus* or *scutellaris* as used by Dutch and other workers who have been considering East Indian material.

Aedes (*Stegomyia*) *marshallensis* Stone and Bohart from Kwajalein, Namarik and Ebon Atolls and Kalli Island in the Marshall Islands.

Aedes (*Stegomyia*) *guamensis* Farner and Bohart from Guam.

The authors state that their studies of collections from Melanesia, Micronesia and Polynesia indicate that the species *pseudoscutellaris* is confined to Polynesia.

and that the range of non-periodic filarinas is coincident with the combined ranges of *pseudoscutellaris* and *longae*.

ii. *Aedes* (*Stegomyia*) *kenillii* n. sp. from Ulithi Islands, Western Caroline Islands is described. It is a member of the *scutellaris*-group and would, in the nomenclature of Edwards 1932, be referred to as a variety of *scutellaris* Walker (= *variegatus* Dolschall of Edwards 1926) John Smart

OLSON T. A. & KEEGAN H. L. The Mosquito Collecting Program of the Seventh Service Command for 1942-1943. *J. Econom. Entom.* 1944 Dec., v 37 No. 6 780-85

EDNEY E. B. Laboratory Studies on the Bionomics of the Rat Fleas, *Xenopsylla brasiliensis* Baker and *V. cheopis* Roth. I. Certain Effects of Light, Temperature and Humidity on the Rate of Development and on Adult Longevity *Bull. Entom. Res.* 1945 Jan., v 35 Pt. 4 399-416 2 figs. [22 refs.]

It is generally agreed that epidemics of bubonic plague occur under conditions which allow rapid breeding of fleas and long periods of survival apart from the host. The estimation of the longevity figures is important, therefore, in the prediction and control of such epidemics. In the past, attention has been centred mainly on the effects of saturation deficiency on the larvae and adults, and the results obtained by different workers have varied considerably. In the present investigation, the author's main object was to ascertain whether other important factors are concerned in longevity and, if so, to ascertain to what extent these explain the differences referred to. Since in the past, little attention has been paid to the effects of light, this aspect receives special attention, and a considerable part of the paper is devoted to it. The work was carried out during the period December 1941 to June 1944 in Uganda. The experiments were made in a dark room in the laboratory where the effects of humidity and light were studied under controlled conditions but where it was not found possible to control the temperature accurately throughout the work. The significance of the results obtained, however, was not greatly diminished, since control series of fleas were kept at the same time for comparison of the effect of other factors. The following is the author's summary —

"1. The effect of light on adult longevity and on the duration of pre-adult stages and the effect of psychrometric (humidity) conditions during pre-adult stages upon adult longevity were investigated in *Xenopsylla brasiliensis* and *V. cheopis*.

"2. In no experiment was a significant difference found between the two species but the figures shown are those for *brasiliensis* only as the numbers of *cheopis* were small.

"3. Light reduces slightly the longevity of unfed, wild-caught adults, and of unfed laboratory bred adults. It reduces considerably the duration of all pre-adult stages. It is suggested that this is due to radiant heat.

"4. If fleas are anaesthetised while being removed from their hosts, the mean longevity is significantly reduced.

"5. It was confirmed that wild-caught females live longer than males, that the cocoon stage of females is shorter than that of males under all conditions used, and that newly emerged, unfed adults show no difference in longevity between the sexes.

"6. Eggs fail to develop at 24°C. If the saturation deficiency is 10 mm. Hg or more below this saturation deficiency has little or no effect upon the duration of the egg stage.

"7. At 80 per cent. relative humidity all the pre-adult stages are shorter at 35°C. than at 24°C. If all the adults are kept in the same conditions, those

resulting from pre-adults kept at the higher temperature live for a shorter period than those resulting from pre-adults kept at the lower temperature

8 At 24°C. the larval period increases from 12.4 to 25.1 days as the saturation deficiency increases from 2.3 to 8.8 mm Hg but this range of saturation deficiency has no effect upon the duration of the cocoon stage

9 Saturation deficiency during the pre pupal stage is shown to bear a linear relationship to adult longevity

10 The results obtained by previous workers are discussed in the light of the present work and a possible explanation is suggested for certain discrepancies that still exist

This interesting paper contains much detailed information which does not lend itself to summary and the work should be consulted in the original by those interested

R M Gordon

ZUMPT F *Rhipicephalus sanguineus* Latreille und andere krankheitsuebertragende *Rhipicephalus* Arten. [*R. sanguineus* and other Disease Vectors of the same Genus.] *Deut Tropenmed Ztschr* 1944 Feb-Mar v 48 No 3-6 117-23 11 figs

This paper presents a general account of the tick genus *Rhipicephalus* and discusses its medical and veterinary importance and the control measures which should be adopted when infestation occurs

The features which distinguish the genus from other genera of Ixodidae are listed and the distribution of the 40 known species is briefly discussed. *R. sanguineus* which is almost cosmopolitan in the warmer lands is taken as a type and its anatomy is described and illustrated. The characteristic features of the following medically important species are given briefly—*R. appendiculatus*, *R. simus*, *R. capensis*, *R. bursa*, *R. cecati* and *R. pulchellus*. All but the last resemble *R. sanguineus* in colour and general appearance. As in the case of all Ixodidae there are two larval stages—a six legged larva and an eight legged nymph

The life-history of *R. sanguineus* under typical conditions is set out. The duration of the various stages at specified temperatures and their resistance to starvation are given. Although under the most favourable laboratory conditions the life-cycle may be completed in 76 days in nature in sub-tropical regions there is probably only one generation each year

The more important diseases of man and animals transmitted by these ticks and their distribution are briefly discussed in a short section on each disease. Some 16 diseases are dealt with in this way including North African relapsing fever and the tick borne typhus group

Finally there is a short section dealing with control measures. It is important to keep domestic dogs free from ticks otherwise they may become established in houses. The dogs may be freed from ticks by bathing in 3 per cent Creolin or carbolic soap or treated by rubbing the coat with spirits of camphor and water. Derris powders are also effective. When a house has become infested fumigation is often the only remedy. For scouring a 5 per cent cresol or lysol soap solution may be used. Cattle are commonly treated by dipping

W A L David

EWING H E The Trombiculid Mites (Chigger Mites) and their relation to Disease. *J Parasitology* 1944 Dec. v 30 No 6 339-65 8 figs. [Numerous refs.]

The paper the contents of which are indicated in the title is a summary of some aspects of present-day knowledge

The author describes his own experience in rearing the common N American chigger mite now known as *Entrombicula alfreddugesi*. A point of interest

is that the larva commonly feeds on turtles and toads as well as mammals. The approximate geographical distribution of that species and of three other important species (*T. andersoni* of Europe, *T. deliensis*, India, East Indies, Queensland, *T. akamushi* Japan to Malay Peninsula) is shown on a map.

The paper includes a revised key to genera of Trombiculid larvae of the world, and some notes and figures on points of taxonomic importance.

There is an interesting section on the pathology of the larval bite and the human reaction. The account of the relation of *Trombicula* to scrub typhus, and the section on protection, are not of great value. The bibliography is up to date.

P. A. BURTON

LABORATORY PROCEDURES

MACMAHON H. E. & DELVECHIO S. B. A Simple Technic for Rapid Sectioning. *New England J. of Med.* 1944 Dec. 14 v 231 No. 24 794

The rapid examination of tissue at the time of a surgical operation is usually made with frozen sections and this involves the use of a considerable amount of equipment. The following simple method has been used at the Cambridge Hospital, Massachusetts U.S.A., for over a year. All the equipment required is a safety razor blade, a prepared stained slide, a clean slide and a clean coverslip. Slides are coated with Mayer's albumin-glycerin mixture, dipped for a few seconds into a 1 per cent. aqueous solution of toluidin blue, drained and allowed to dry.

Cut a thin section that can be easily handled. Holding the section on the blade, gently place it on the ball of the finger. Draw the stained slide lightly and quickly across the section, staining only one surface of the tissue. Immerse the tissue in water. Mount the tissue on a glass slide with the stained surface up. Place a coverslip over the section and with a good light examine the tissue.

This method has been compared with the usual freezing method, and also with permanent sections with the same pieces of tissue—mammary gland, lymphatic gland, endometrial curetting tissue, uterine cervical tissue, and rectal mucous membrane. "In no case did the frozen section or final report conflict with the original rapid section diagnosis."

J. F. CORSON

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS.

- I. BLACKLOCK, D. B. The Population Problem of India. *Brit. Med. J.* 1943 Dec. 23 805-7.
- II. BARROW, M. Population Problems of India. [Correspondence.] *Ibid.* 1944 Jan. 15 95.
- III. MEGAW, J. W. D. India's Population Problem. [Correspondence.] *Ibid.* Mar. 4 335.

I. Professor Blacklock notes that the population of India (1941) was about 247 persons to the square mile, and that the vast bulk of the people live in villages. In 1831 the population had increased by 40 per cent. over that of 1831 and in 1941 an increase of about 15 per cent. over 1831 was recorded. The public health of India is poor and the death rate is high. If as a result of enlightened land policy and improvement in public health the social conditions of the Indians become greatly improved, it seems inevitable that eventually there will be overpopulation even for the more productive land, and consequent starvation. The prospect of this situation calls for political and economic planning, but it is impossible for medical men to accept any suggestion that

limitation of population by disease should be allowed to continue if the means for prevention or cure could be applied. The author mentions other checks on population—war, infanticide—which have operated but which perhaps may be avoided in the future and is driven to the conclusion that the solution of this urgent population problem will lie in some form of birth control. He adds a warning that the situation is likely soon to develop to a critical point and that a course of action must be decided early. It will not bear much delay.

ii. In a letter commenting on Blacklock's paper BARROW quotes evidence which shows that at the present time India produces enough food to give 88 per cent of the population a daily ration of 2,800 calories if none was exported and if there were no maldistribution. Proper utilization of land would mean that the country could produce nearly 4½ times as much food which should be enough for a population three times as great as that which exists at present.

iii. In a contribution to this discussion Sir JOHN MEGAW criticizes the figures given by Barrow as fantastically optimistic and in general support Blacklock's views. The solution of the problem lies in increasing the production of food and in regulating the rate of reproduction of children so as to maintain a satisfactory balance between food supply and population.

These papers should be read in conjunction with that by NOTESTEIN below.

NOTESTEIN F W Problems of Policy in relation to Areas of Heavy Population
Pressure *Milbank Memorial Fund Quarterly* 1944 Oct. v 22 No 4
424-44 Charles Wilcocks

In his discussion of this complex subject the author takes certain countries as examples of those parts of the world in which rapid increase of population has taken place and which may in a relatively short time become so overpopulated in relation to their present means of production that very grave sociological results would be inevitable. India for instance would double its present population (400 millions or so) in 57 years if the trends of 1921-1941 continued. Java would do the same in less than 40 years and the Philippines in 32. Similar situations exist in many other parts of the world especially among those peoples who are technologically undeveloped. Unless there are drastic changes sooner or later there must come a point at which continued increase forces down living levels so that mortality will begin to rise. The limits of agricultural improvement were virtually reached in Java in 1930. The limits of agricultural

The author considers possible methods by which this overcrowding may be prevented. Emigration, even if successful would effect no more than temporary alleviation to allow mortality to increase would offend the humanitarian attitude of enlightened people and would not succeed. Birth control is not a method which commends itself to primitive people whose social structure aims at preservation of the family or group rather than of the individual. More advanced peoples whose outlook is more individualistic have succeeded in restraining their own multiplication in spite of low mortality and the author concludes that the welfare of the less developed peoples in this respect rests upon a programme which will bring about a decline of fertility by improving standards of living, urbanization, widespread education and growing contacts with foreign cultures. The first effect would probably be to increase population pressure but there would follow a decline in fertility which would in due course form a balance with the decreased mortality which these measures would achieve. The subject touches upon public health in that the author believes that only a society in which the individual (child or adult) has a reasonable chance for survival in healthy life will develop that interest in the dignity and material well being of the individual essential to the reduction of fertility. Public health should therefore be fostered as part of a programme to reduce growth potential.

Agricultural, political and social development (such as the breaking down of caste and other barriers) are essential parts of the programme outlined.

Charles Wilcocks

VINT F W. Solar Rays. Facts or Fiction? *East African Med J* 1944 Aug v 21 No 8 227-39 [84 refs.]

In this paper Vint has made a survey of the possible effects of the sun's rays on the living organism as a preliminary statement bearing on the physiology of the African. He was prompted to this by the realization that no satisfactory explanation has yet been given of the lack of development of the African, and he took as his starting point the fact that the African has a black skin.

Pigmentation which develops as a result of exposure to the sun is said always to be extracellular and Vint has seen extracellular pigment in Africans and sees no reason why a light-skinned African should not develop extra pigment. [The demarcation of areas of skin usually covered by clothing, from those usually exposed to the sun, is often very clear in black skins in Africa.] Black surfaces absorb more heat than white surfaces and the heat thus taken in is lost by evaporation of sweat. It has been stated that in the coloured races there are more sweat glands than in the white races, and that there is a richer blood supply in the skin. The sweating mechanism works more economically in the black races but adaptation to tropical conditions though good, is not complete and heat stroke is by no means unknown in Africans.

Vint discusses at some length the physiology of sweating and the importance not only of loss of fluid but also of loss of salts in this process. The production of histamine by the skin probably increased if the skin is injured, may be a factor in tropical physiology. Histamine provokes the secretion of acid in the stomach, and it has been said that the normal Indian has a higher gastric acidity than the normal European. pernicious anaemia is rare in the tropics. Histamine provokes tissue breakdown, and it is perhaps possible that an over-production of histamine due to exposure, may be a factor in the under-nourishment of the African living on a border-line diet.

In a hot climate the basal metabolism is reduced. the thyroid gland is minutely concerned in metabolic activity and KERR has stated that the dweller in Eastern Asia belongs to the hypothyroid race. [The assumption is that the same may be true of the African.]

Vitamin D is formed by the photochemical action of ultraviolet light on the sterols. it is formed on not in, the skin, and it has been said that food is not generally an important source of this vitamin, but that it is taken into the body (in animals and birds) either by ingestion from the skin (as in licking or preening) or by absorption through the skin. Certainly rickets is rare in Africa, and the reason probably is the formation of vitamin D by the action of sunlight on the excreted fatty material of the skin. It has been said that removal of the thymus increases the severity of rickets in animals, and decreases the effect of vitamin D. Vint has noticed that a persistent thymus is a very common finding at autopsy in Kenya.

Reviewing these facts and theories the author maintains that a case has been made for "a complete investigation of the physiology of the African before any other researches are carried out as to the cause of his lack of development.

Charles Wilcocks.

DEMBOVITZ N. Psychiatry amongst West African Troops. *J Roy Army Med Corps*. 1945 Feb., v 84 No 2, 70-74

The author an Army psychiatrist working among West African troops in India, stresses the importance of a working knowledge of the social life, habits, beliefs and customs of an individual's social group if the significance of any

unusual behaviour or thought is to be adequately assessed. In the first part of his paper he describes those aspects of personality which are common to nearly all West Africans as well as individual differences of the main ethnological and geographical sub-groups. He then refers to the special problems in management which these personality features present. The third part of the paper enumerates and describes various psychiatric symptoms and syndromes commonly seen in these peoples and he concludes by describing the therapeutic measures which he has found to be appropriate.

The West African is an easy-going unambitious ingenuous individual possessed of a child like simplicity and humour—like a child closely tied to his parents and his brothers. He is child like in his emotional responses reacting sharply to any imagined attack upon his rights easily influenced by the attitudes of his group highly superstitious and obeying the laws of his Juju meticulously and without question. The educated boy tends to be more litigious and less contented than his uneducated fellow. In India the West African makes a reasonable adjustment although he tends to become more excitable and irritable. General intelligence is low when assessed by European standards—a score of 20 (S.G.5) on the standard Raven's Progressive Matrices test is the average (although European norms for such a test are scarcely appropriate)—but certain specific aptitudes such as mechanical, sense of locality etc. are fairly high.

From a psychological as well as a physical and ethnological viewpoint West Africans may be divided into two main groups—Northern Territory men comprising the Hausas Fulanis and pagan tribes of the northern territories of the Gold Coast and Nigeria and secondly the Coast Africans consisting of a large group of linguistically separate tribes inhabiting the coastal areas.

The Northern Territory men are first class fighting soldiers with their good physique their courage their pride in arms and their amenability to discipline. They have some Arabic ancestry and the dominant Fulanis and Hausas are Mohammedan while the indigenous tribes remain pagan. They share a common language and form small agricultural communities each under its own chief. All believe in Juju but they are much less concerned with magic practices than the Coast Africans of the South. They present few special psychiatric problems.

The Coast Africans form many separate tribes each with its own culture and social organization traditionally at war with each other and speaking mutually incomprehensible languages. Whatever their professed religion they are pagan at heart and are bound together in their fanatical belief in Juju—the conferring of magic power for good or evil on an inanimate object by a ceremony. Juju is invoked in every mental upset whatever befalls a man is due to an angry Juju which has been placed within him. In their rich folklore is implicit the belief in the power of the dead over the living and in the existence of various supernatural beings. The preoccupation with magic practices the existence of numerous secret societies (many of which are widespread and anti-social) the occasional occurrences of cannibalism and human sacrifice (many of the criminals being the semi-educated townsmen) present problems both disciplinary and psychiatric.

Next are described various problems in man-management provided by the West African: a poor intelligence his child-like and egotistical emotional attitudes his lability of mood and the cultural setting from which he has come.

The author then details the psychiatric syndromes which are of special frequency. Hysterical states are frequent and dramatic and the hysterical mechanism is so readily employed that conversion symptoms colour not only neurotic depressions and anxiety states but also true psychoses. Hysterical reactions are invariable in mental defectives. Psychopathic personalities with anti-social trends are a special problem with their ready resort to violence and great physical strength. Running amok is not uncommon in manic and

schizophrenic reactions, in epilepsy psychopathic personality acute trypanosomiasis and cerebral malaria the picture is one of a man suddenly seizing a Tommy gun and rushing round slaying all he meets. Hallucinations are of little significance normal West Africans see and speak to their dead parents, and terrifying hallucinations are common in anxiety and hysterical states of good prognosis. Trypanosomiasis accounts for over 10 per cent. of acute mental illness—often diagnosed as acute mania or catatonic schizophrenia before c.s.f. investigations reveal the true pathology—and lumbar puncture should be performed on every psychotic patient. "Recurring confusional state" apparently hysterical, of about a month's duration and recurring at a particular season every year is a special condition found in West Africans the attack ceases spontaneously in its natural time and the West African abroad tends to pass into a Ganser state at the conclusion of each attack.

The precipitating factor in psychoneurotic states is commonly obvious and trivial—an imagined insult or an undeserved sentence may be the sole precipitating factor in a severe condition—and the illness clears up dramatically if such environmental factors can be dealt with successfully. Hysterical symptoms respond well to strong positive suggestion of a crude sort whereas the response to hypnosis or narco-hypnosis induced by Europeans is poor. The management of psychotics is on orthodox lines. Sedatives are effective only in very large doses—for example one grain of morphine with 1/20th of a gram of hyoscine or ten drachms of paraldehyde. The author has found occupational therapy useful in certain cases.

James Milne

CAMERON T. W. M. On the Centenary of the Birth of Patrick Manson, the Father of Modern Tropical Medicine. Reprinted from *McGill Med. J.* 1944 Oct., v 13 No. 6 14 pp.

In this address Professor T. W. M. Cameron has reviewed the outstanding events of the life of Sir Patrick Manson on the occasion of the centenary of his birth (October 3rd 1844) and has taken advantage of this notable occasion to compare his career with that of another great pioneer Sir William Osler. It is also revealed that it was due to the initiative of the latter in a letter dated February 3rd, 1907 that the question of a school of parasitology in McGill University was first raised, a proposal which eventually resulted in the establishment of the Institute of Parasitology at Macdonald College P. Q.

In this manner we are introduced to the new diploma in tropical medicine of McGill University of which this Institute forms one of the foundation stones. It will be responsible for the laboratory didactic instruction on tropical diseases. The other basic subjects will be public health, preventive medicine and clinical instruction in diseases common in the tropics, but this diploma will contain one important innovation in the teaching of tropical medicine, for at least part of the clinical instruction will take place in the tropics a course which has now become practicable when Trinidad may be reached by aeroplane within twelve hours. It seems quite logical after preliminary instruction in the laboratory on the aetiology pathology and prevention of tropical diseases to repair to those countries where these diseases exist, and there under experienced practitioners, to apply the facts and procedures learned in Canada.

Sound training in general principles of public health and preventive medicine should provide the physician proceeding to the tropics with a secure foundation and should assist him in attaining the ideals set forth in Osler's address to Manson's students at the original London School of Tropical Medicine in 1909.

P. Manson Bahr

BOOK REVIEWS

KNIGHT K. L. BOHART R. M. & BOHART G. E. **Keys to the Mosquitoes of the Australasian Region including a Synopsis of their Distribution and Breeding Habits.** 71 pp. National Research Council. Division of Medical Sciences. Issued by the Office of Medical Information (Under grant of Johnson & Johnson Research Foundation.) Washington 1944 July

In this paper the Australasian region is regarded as including the Tuamotu Archipelago in the East and the Marianas and Hawaiian Islands in the North. Species from the Moluccas are included in order to cover the possibility of oriental species found there extending to New Guinea but not yet having been recorded from that island. New Zealand, Tasmania, Victoria, South and West Australia are excluded from consideration as being without the main area of current military interest.

The paper, which is a duplicated product, not a printed work, contains a key to the tribes of Culicidae taken direct from EDWARDS (1932) (*Genera Insectorum* Fasc. 194), a key to *Bironella* modified from SWELLENGREBEL and RODENWALDT (1932) (*Die Anophelen von Niederländisch-Ostindien* Fischer Jena), a key to the species of *Anopheles* taken partly from RUSSELL ROZEBOOM and STONE (1943) (*Keys to the Anopheline Mosquitoes of the World* Amer. Ent. Soc. Philadelphia Pa.) keys to the genera and to the species therein. The latter keys are mainly applicable to females though not entirely so; a table giving the larval habitats where known is included but there are no keys to the larvae.

The generic concepts used are the broad ones of EDWARDS (1932) but the authors have keyed out the species contained in these genera without keying out the sub-genera. This simplification is carried to the length of combining the species of *Armigeres* and *Aedes* in one and the same key. It thus comes about that specimens of a sub-genus passed through the key may not key out together or in a manner that points to their relationship. Furthermore should specimens that happen to represent a new sub-genus come to hand—and STONE & BOHART (1944 *Proc. Ent. Soc. Washington* v 46 205) have recently erected two new sub-genera within the genus *Aedes* for Australasian species—the position in the key to which such specimens will pass gives no positive indication of the relationships of the new sub-genus.

The authors follow RUSSELL ROZEBOOM and STONE in using trinomial names thus indicating that they regard the forms usually designated by the non-committal if ambiguous term variety as sub-species. They limit their remarks on zoogeography to a quotation of 14 lines from EDWARDS's (1924 *Bull. Ent. Res.* v 14 351) paper on the Mosquitoes of the Australasian region. EDWARDS in 1924 (*loc. cit.*) dealt with 145 species; the present authors deal with 238 species and sub-species but they candidly admit that they have seen specimens of only about half of these and that their paper is to be regarded as of a preliminary nature.

John Smart

TAYLOR F. H. **The Intermediary Hosts of Malaria in the Netherlands East Indies.** Commonwealth of Australia Dept. of Health Services Publication (School of Public Health and Tropical Medicine) No 5 (Second Edition) 1944 Oct. 30 100 pp. With 24 figs., 1 graph & 16 maps. Glebe New South Wales. Australasian Medical Publishing Company Ltd. Seamer and Arundel Streets.

The first edition of this publication was issued in 1943 [reviewed in this *Bulletin* 1944 v 41 698] and the fact that a second edition has had to be issued in less than a year's time proves its usefulness.

The first edition ran to 85 pages. The additional pages in the second edition are taken up with descriptions of *Anopheles hyrcanus* Pallas (the typical form) and *Anopheles hyrcanus* X *Venustus* and with "Notes on the Distribution of Malaria" by Dr R. E. Murray (10 pages and sketch map).

Apart from the new matter mentioned above the second edition does not differ from the first.

John Smart.

GASCHEN H. [Dr. ès Sciences chef de travaux à l'Institut d'Hygiène Lausanne (Suisse)] Les Glossines de l'Afrique Occidentale Française. [The Tsetse Flies of French West Africa.]—*Acta Tropica* Basel. 1945 Suppl. 2, 131 pp. 114 figs. & 1 folding pl. [Bibliography.]

In the introduction by ROUBAUD it is stated that this book on the tsetse flies of French West Africa is intended for administrators missionaries doctors hygienists, farmers and business people.

After listing 21 species and eight varieties the author briefly describes the general anatomy of the fly. The main section of the book, consisting of about 60 pages, contains a key for the identification of the 12 species which occur in this part of Africa, detailed descriptions of the species, line drawings of differentiating characters and maps showing their distribution. Those occurring in other parts of Africa are dealt with in less detail. Habits, haunts and relation to disease are noted for each species but are more generally discussed in a chapter dealing with biology. To conclude the author mentions some of the measures used for the control of the tsetse fly and describes certain methods for collecting, dissecting and examination.

There is a short glossary of entomological terms at the end of the book, a hundred or so references to the literature by French, British and a few German authors and a large, folding, illustrated key to the local species of *Glossina*.

This is not a work for the advanced student but is a useful introduction to the subject and a handy book of reference for those for whom it was written.

H. S. Lesson

HELANDER E. V. Über die Magensekretion bei Bothriocephalusträgern. [The Gastric Secretions in Persons harbouring *Diphyllobothrium latum*.] *Acta Med. Scandinavica*. 1945 Suppl. 155. 115 pp. 2 figs. [Bibliography.]

In view of the similarities in the blood of those suffering from idiopathic, spontaneous or better cryptogenetic pernicious anaemia and the severe form of anaemia which may arise in some of those who are infested with *Diphyllobothrium latum* and in view of the changes in the gastric secretions in the former it is well that we should know whether the like changes occur in the latter. Therefore in spite of the fact that no striking alterations have been found and the results of this investigation are largely negative the time spent on it cannot be regarded as wasted. [We should remember also that though severe anaemia may occur in those harbouring this cestode many persons are infested without exhibiting any profound alteration in the blood.] The work must have been somewhat tedious but it has been carried out with thoroughness and should therefore not need to be repeated.

Apart from a short introduction and a brief summary the report of the work is divided into ten chapters. In his introductory remarks the author states that infestation with *Diphyllobothrium latum* is common in Finland, where the study has been undertaken. Records have been published showing that 20-25 per cent. of the inhabitants of parishes near the coast and 40-50 per cent. and even more in the eastern parts are infested. Symptoms are often mild and vague

sensations of fulness in the epigastrium hunger and general discomfort with craving for salty foods glossitis diarrhoea lasting for a few days feelings of faintness perhaps paraesthesia of the hands.

In the first chapter is considered generally the question of gastric secretions and anaemia with abundant quotation from the literature noting particularly the achylia common in cryptogenetic pernicious anaemia. The author quotes WEINBERG as saying that in families in which cases of pernicious anaemia occur other members may show a reduction in the normal HCl content of the gastric juice [but does not state that these might be in an early stage of the disease]. In both cryptogenetic pernicious anaemia (to save space and repetition we shall henceforth call this c.p.a.) and *Diphyllobothrium* anaemia (in future D.p.a.) signs of gastritis with atrophic histological changes may be seen more in the fundus than at the pylorus. Several authorities have stated that the intrinsic factor is deficient or lacking in c.p.a. though free HCl is present but that total gastric secretion is reduced. In D.p.a. the intrinsic factor is probably always present but it is possible that the supply of the anti-anaemic principle in the liver is exhausted or its utilization prevented.

In the second chapter the author sets out the problems which he proposes to solve at least to tackle. Hitherto in worm-carriers the investigation of the gastric function has been mainly confined to the question of secretion of HCl. He sets out to determine the following—(1) The hydrochloric acid. (2) The total chlorides. (3) The intrinsic factor (4) The pepsin. (5) The secretion of the gastric juice (6) Whether the amount of the intrinsic factor is quantitatively reduced in D.p.a.

The next chapter is concerned with the methods in general use for carrying out gastric analyses and in particular the TAYLOR and LASCH reaction for estimation of the intrinsic factor. One method which the author uses must be given in a little more detail because in subsequent chapters and in the discussion he frequently uses terms which he here defines. For making fractional tests after the patient has fasted for 10 hours a fine sound is passed to a distance 40–50 cm. from the teeth and the stomach contents are withdrawn—these are the resting content (*Ruheinhalt*) after an interval of 10 minutes suction is again carried out three times and the material obtained he calls empty secretion (*Leerssekret*). A drink of caffeine 0.2 gm. in 300 cc. of water with addition of two drops of methylene blue solution is then given through the sound and every ten minutes thereafter 15 cc. are withdrawn until the colour disappears. The gastric juice so obtained is called the after-secretion (*Nachsekret*) and the time between the giving of the fluid and the disappearance of the blue colour is the emptying time (*Entleerungszeit*). The different amounts withdrawn are examined for estimation of HCl and total acidity and can be added together. In those whose *Leerssekret* does not give a positive Congo-red reaction and at least after 30 minutes from the taking of the fluid 16 units of insulin are injected intravenously or if the vein is hard to find or unsuitable, 0.1 cc. of histamine per 10 kgm. body weight subcutaneously. The methods of estimating the HCl total acidity total chlorides intrinsic factor pepsin etc. are detailed.

The author next states the nature of his investigation material. This comprised 51 carriers of *Diphyllobothrium latum* 25 females 26 males between 18 and 45 years of age 23 patients with pernicious anaemia of whom 17 were harbouring the worm and 30 normal persons 21 women 9 men 17–44 years old. He also planned to keep the worm-carriers under his observation for two months after the worms had been got rid of and the pernicious anaemia patients after remission. When their worms had been expelled several of the sufferers feeling well refused further investigation so only 20 could be subjected to subsequent examination.

The two following chapters are concerned with the gastric secretion and its constituents in normal subjects. First, the records of others already in the literature, and then the author's own findings details being presented in series of protocols which are summarized below. After this, the secretion in *Diphyllobothrium* carriers which is the title chosen for the whole work, is treated in a similar manner one chapter being concerned with a recording or summarizing of earlier work and another with the author's own findings in a series of protocols with explanatory letterpress. Chapter IX goes over the same, or rather similar ground with cases of pernicious anaemia, those with worm infestations, before and after remission, and then cases of cryptogenetic pernicious anaemia.

The results may be summarized as follows.—In cases of pernicious anaemia and in those harbouring *Diphyllobothrium latum* there are variations in the gastric secretions quantitatively within the limits regarded as those of health. Earlier studies have proved that, as regards gastric acidity there is no marked departure from the normal and there is no difference in the two sexes. [Previous investigators have recorded their results in the sexes separately the author finding no practical difference, has dealt with the subject as a whole and not split them into two sex-groups.] The variations in the gastric secretion as a whole and in its constituents have (with one exception among 20 cases) been within the normal limits. Studies carried out on the same person on successive days have shown that the acidity and the amount of pepsin present may vary. Only after many fractional removals have been carried out on worm-carriers, before and after removal of the parasite, and comparing the averages so obtained can we give any satisfactory answer to the question whether the presence of the worm has any effect on the gastric secretion. He finds the differences in these averages too slight to warrant any definite answer. Moreover if we compare the findings in worm-carriers with those in the healthy we get the same results. Ten out of 30 healthy subjects and 14 out of 41 carriers of the worm showed so long a delay that 30 minutes after taking the test-drink there had been no secretion of free HCl. The average values in carriers and in the healthy after the giving of insulin or histamine, differed no more than in those who had not received either. Of 51 carriers three still had achylia, but none of the healthy. The average amounts of acid, total chlorides and of pepsin in the carriers after insulin or histamine were below those of healthy subjects who had been given insulin. Mucus was present just as often in the healthy as in the carriers. The average amount of secreted juice in carriers not receiving insulin or histamine was somewhat higher than in the healthy—it was as if the presence of the worm had a stimulating effect on the gastric secretion.

The time of emptying the stomach was usually shorter in carriers than in the healthy. The average of the intrinsic factor reaction was not much different from that in the healthy. In the majority of the author's worm-carrying patients the total amount secreted was greater than in the healthy but in a minority it was definitely lower—hence not much stress can be laid on this. In all the cases of c.p.a. insulin-negative achylia was found both before and after remission. Of 17 D.p.a. cases 15 showed insulin negative achylia and after remission [presumably removal of the worm] 10 of the 17 showed the same. Total chloride estimations yielded similar results—some cases of both groups of anaemia (c.p.a. and D.p.a.) gave an amount lower than, others an amount equal to that of the healthy. But the average total chloride concentration which rises somewhat after a remission, is still definitely lower in the healthy and in the c.p.a. cases than in those of *Diphyllobothrium* origin.

Digestive pepsin shows similar variations. Cases in which it was lacking were found in both forms of anaemia. Prior to remissions the amount of pepsin in c.p.a. does not reach the level of the healthy subject, whereas in some of the

D p a. cases it does. The intrinsic factor reaction in c.p a. he found somewhat higher than in the healthy — it is higher also than in cases of D p a. By Taylor's method of estimating this factor the stomach in some c.p a. cases at least after insulin stimulation can secrete as much as a healthy organ — in others however the quantity is distinctly less because of the reduced total amount of gastric secretion. It is known that in c.p a. the stomach is dry and that maintaining its secretion without insulin or histamine stimulation is difficult. Earlier researches had recorded that in c.p a. the intrinsic factor of the gastric content was not diminished but that the total amount was less because the secretion as a whole was reduced and the author thinks it is more probable that we have to do with a functional inadequacy of the glands secreting the intrinsic factor.

We have given in the foregoing an analysis of the author's statements as fully as we can — as the subject is an important one to have once for all settled. They are often vague and obscurely worded. It will perhaps make the results a little clearer if we give the author's conclusions in his own words (translated). After stating that in those harbouring this worm the stomach is usually emptied more quickly than in normal subjects he says —

1 Of 51 *Diphyllobothrium latum* carriers three had insulin or histamine-negative achylia — in 11 (of the 51) the HCl and the total acidity were less — but in the majority they were somewhat raised.

2. The total chlorides in a minority (14 out of the 51) were reduced, in a great majority somewhat increased.

3 Assuming that Taylor's method is reliable the intrinsic factor is not reduced in the worm-carriers.

4 In 14 of the 51 pepsin digestion was somewhat reduced — but in the majority it was somewhat increased.

5 In a minority (14) the resting content *Leersektet* and *Nachsektet* were less — in a majority the *Leersektet* was equally large and the resting content and *Nachsektet* greater.

6 In pernicious anaemia due to *Diphyllobothrium latum* the gastric secretion contains as much as and in other cases [? c.p.a.] more intrinsic factor than is found in healthy subjects.

It is difficult to account for these varying results. It may be that the *Diphyllobothrium* toxin acts reflexly or directly on the blood vessels of the gastric glands and that according to the mode of reaction and perhaps also the resorption in the intestine the stomach secretion is reduced in some of the cases — is increased in a majority and remains unchanged in others. [If this is not mere tautology it is totally unenlightening.] Also the increased gastric secretion and increased acidity would explain the sensations of hunger in worm carriers. The average amount of *Leersektet* and of *Nachsektet* after insulin is reduced both in cryptogenetic and in *Diphyllobothrium* pernicious anaemia. Accordingly the total amount of intrinsic factor secreted in pernicious anaemia is reduced. In a few cases of pernicious anaemia the amount of *Leersektet* and of *Nachsektet* after insulin administration and the total amount of the intrinsic factor may be as much as in healthy subjects.

With findings so variable values being sometimes higher sometimes lower than sometimes equal to those of healthy subjects one can only sympathize with the author in the barrenness of the reward for so much work. The important fact which does emerge is that no reliance can be placed on gastric analysis in interpreting the effects of the presence of this cestode in man.

H Harold Scott

MOZLEY Alan [D.Sc. (Edin.) F.R.S.E.]. The Control of Bilharzia in Southern Rhodesia. 307 pp. 1944 Salisbury Southern Rhodesia.

This book deals mainly with the biology distribution and control of the two species of molluscs serving as bilharzial intermediaries in Southern Rhodesia. *Planorbis globosus* transmitting *Schistosoma haematobium* and *Biomphalaria pfeifferi* (formerly *Planorbis pfeifferi*) transmitting *S. mansoni*. It would appear (p. 31) that *P. globosus* is the more widespread, as BLACKIE found in 1932 (this Bulletin 1932, v 29 401) and that the two species are associated with each other and with a considerable degree of pollution of their habitats. The sparseness of limestone rocks, the low organic content of most soils, and the long periods of drought in the country are all factors unfavourable to these snails and indeed, the two vectors tend to be restricted to small man-made pools polluted with organic matter residual pools in the bed of intermittent streams, and small perennial streams, mostly on the High and Middle Veldt. Aquatic vegetation or a bottom of organic mud is a necessary part of the habitat. Schistosomiasis is increasing in the country and, in Mozley's view control of the intermediaries is both highly desirable and largely practicable.

The greater part of the book (pp. 32-230) is a list of sampling points on streams and in pools, classified under drainage areas and containing notes on all molluscs found this will doubtless be of use if a control campaign is undertaken. There are also some full chemical analyses of pool and stream waters of snails, and of their shells. Another long section (pp. 233-280) dealing with chemical control mainly describes the successful use of the mineral basic copper carbonate, Malachite. This mineral has its low solubility increased by plant acids and by the saponin-containing powdered dried pods of a common tree *Sesbania madagascariensis*. This powder is itself toxic to snails, as are also various extracts of other plants *Tephrosia virgin*, *Eucalyptus* sp. *Copaifera mopani*, and *Picrocarpus angolensis* ("Mukwa"). Malachite mixtures promise to be both effective against snails and harmless to mammals.

While the book contains a mass of useful data, they are largely undigested and loosely thrown together. Thus, the chemical control section consists of tabulated laboratory notes in which there is no way of finding (say) what malachite mixture to use without searching the tables line by line. And it is not clear whether the 189 pages of habitat notes are summarized inadequately on pp. 31-32, or not at all.

B. G. Peters.

BUREAU OF HYGIENE AND TROPICAL DISEASES

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[No 7

A LIST OF ANOPHELES CONCERNED WITH TRANSMISSION
OF DISEASE IN MAN

Compiled by JOHN HULL GRUNDY

Royal Army Medical Corps

Notorious vectors are marked with an asterisk.

<i>Species</i>	<i>Distribution</i>	<i>Disease</i>
1 <i>aconitus</i> Dönitz 1902	Indian and Malayan Orient, Polynesian Oceania (W)	Malaria important vector some areas Filariasis (IV ban- crofti)
2 * <i>albimanus</i> Wiedemann, 1821	C. American, Andean and N Brazilian Neotropica (N)	Malaria a principal vector Filariasis (II ban- crofti)
3 <i>albitalis</i> Lynch Arribálaz, 1878	C. American, Andean, N and S Brazilian and Argentine Neo- tropica	Malaria vector Brazil Filariasis (IV ban- crofti)
4 <i>algeriensis</i> Theobald, 1903	European and Mediter- ranean Palaearctica	Malaria minor im- portance Filariasis (II ban- crofti)
5 <i>amictus</i> Edwards, 1921	Australian Oceania (N)	Filariasis (IV ban- crofti)
6 <i>annularis</i> van der Wulp 1884 (= <i>fuliginosus</i> Giles, 1900)	Indian Malayan and Chinese Orient	Malaria minor im- portance. Filariasis (II ban- crofti)
7 <i>annulipes</i> Walker 1856	Australian Oceania	Malaria minor im- portance.
8 * <i>aquasalis</i> Curry 1932 (= <i>farsimaculatus</i> of some authors)	C. American, Andean (N) and N Brazilian Neotropica	Malaria important vector Filariasis (II ban- crofti) infected in nature.
9 <i>argyritarsis</i> Robineau Desvoidy 1827	C. American, Andean and N and S Brazilian Neotropica	Malaria minor im- portance.
10 <i>austeni</i> Theobald, 1905	C. Trop. Ethiopia	Malaria minor im- portance.
11 <i>baccai</i> Gater 1933	Malayan Orient	Malaria minor im- portance.

	Species	Distribution	Disease
12.	<i>benicrofti</i> Giles, 1902 ...	Polynesian and Australian (N) Oceania	Malaria suspected vector New Guinea. Filariasis (IV <i>benicrofti</i>)
13	<i>barbicostris</i> van der Walp, 1884	Indian, Malayan and Chinese Orient, Polynesian Oceania	Malaria minor importance. Filariasis (IV <i>barbicostris</i> and IV <i>malayi</i>)
14	<i>bellator</i> Dyar & Knab 1906	N Brazilian Neotropica	Malaria important vector Trinidad.
15. ^a	<i>beniensipes</i> (Theobald, 1910)	C. Trop. Ethiopia	Malaria minor importance, Belgian Congo.
16.	<i>clariger</i> (Mengen, 1804) (= <i>bifurcatus</i> Mengen, 1815)	European and Mediterranean Palaearctica	Malaria most important urban vector Palestine, Syria.
17	<i>constantis leucobromus</i> Dönitz, 1902	Mediterranean Palaearctica, N and S. Trop. Ethiopia, S. Ethiopia	Malaria suspected vector S Africa (in winter)
18.	<i>crucians</i> Wiedemann, 1828	Eastern United States Nearctica, Central American Neotropica	Malaria minor importance.
19	<i>crux</i> Dyar & Knab 1908 ..	N and S. Brazilian Neotropica	Malaria doubtful importance.
20.	<i>calidifacies</i> Giles, 1901	Indian Orient	Malaria most important vector Ceylon, important, India.
21.	<i>darlingi</i> Root, 1928	C. American, Andean, N and S. Brazilian and Argentine Neotropica	Malaria important vector Filariasis (IV <i>benicrofti</i>) infected in nature.
22.	<i>ethali</i> Patton, 1905	Mediterranean Palaearctica, Indian Orient (N W)	Malaria suspected vector
23.	<i>cisnei</i> Coquillett, 1902	C. American, Andean and N Brazilian Neotropica	Malaria doubtful importance.
24.	<i>emiliavus</i> Komp, 1941	N Brazilian Neotropica	Malaria doubtful importance
25.	<i>sheriatilla</i> James, 1902 (= <i>lustoni</i> Liston, 1901)	Indian and Malayan Orient, Mongolian Palaearctica (Turkistan)	Malaria important vector
26.	<i>funestus</i> Giles 1900 ..	N and C. Trop Ethiopia, S. Ethiopia	Malaria important vector Filariasis (IV <i>benicrofti</i>) important vector
27	<i>gambias</i> Giles, 1902 (= <i>costalis</i> Giles, 1900)	Mediterranean Palaearctica (sporadic) N and C. Trop Ethiopia, S. Ethiopia	Malaria most important vector Filariasis (IV <i>benicrofti</i>) important vector.

	<i>Species</i>	<i>Distribution</i>	<i>Disease</i>
28	<i>goeldii</i> Rozeboom & Gabaldon, 1941	N and S Brazilian Neotropica	Malaria doubtful importance.
29	<i>grabbamsi</i> Theobald 1901	C. American Neotropica	Malaria minor importance
30	<i>hancocki</i> Edwards, 1929	N Trop. Ethiopia	Malaria important vector where prevalent.
31	<i>hargreavesi</i> Evans, 1927	N Trop. Ethiopia	Malaria important vector where prevalent.
32	<i>hectoris</i> Giacinta Mira, 1931	C. American Neotropica	Malaria minor importance
33	<i>hyrcanus</i> (Pallas, 1771)	Mediterranean Palaearctica	Malaria minor importance
34	<i>hyrcanus</i> Y Venbrua, 1939	Malayan Orient	Malaria important vector Java, Celebes. Filariasis (IV <i>ben crofti</i>)
35	<i>hyrcanus nigerrimus</i> Giles, 1900	Indian Malayan and Chinese Orient, Polynesian Oceania (W)	Malaria important vector some areas, Malaya, Netherlands Indies. Filariasis (IV <i>ben crofti</i>)
36	<i>hyrcanus sinensis</i> Wiedemann, 1828	Indian, Malayan, Chinese and Japanese Orient	Malaria important vector China, S. Japan. Filariasis (IV <i>ben crofti</i> and IV <i>malayi</i>)
37	<i>jeyporensis</i> James, 1902	Indian, Malayan and Chinese (S.) Orient	Malaria vector India, Tonking area.
38	<i>jeyporensis candidensis</i> Koldruml, 1924	Indian, Malayan and Chinese Orient	Malaria important vector south west China, Tonking area
39	<i>karneri</i> (James, 1903)	Indian Malayan and Chinese Orient	Malaria doubtful importance
40	<i>kochi</i> Dönitz 1901	Indian and Malayan Orient	Malaria minor importance, India, Netherlands Indies.
41	<i>leucosphyrus</i> Dönitz, 1901	Indian and Malayan Orient	Malaria Netherlands Indies important in Burma.
42	<i>lindesayi japonicus</i> Yamada, 1918	Chinese and Japanese Orient	Malaria minor importance.
43	<i>*maculatus</i> Theobald 1901	Indian Malayan and Chinese Orient	Malaria important vector Malaya, Netherlands Indies. Filariasis (IV <i>ben crofti</i>) probable vector
44	<i>maculipennis</i> Meigen 1818	European and Mediterranean Palaearctica	Malaria minor importance.

	Species	Distribution	Disease
45	<i>*maculipennis atroparvus</i> van Thiel, 1927	European and Mongolian Palaearctica	Malaria vector Netherlands Spain, Portugal, Maritime Siberia, N Manchukuo and Mongolia.
46.	<i>maculipennis freeborni</i> Arlken, 1936	W United States Ne- arctica, C. American Neotropica (N W)	Malaria most im- portant vector west coast interior Equine encephalitis infected in nature
47	<i>*maculipennis labrancheae</i> Fallenrod, 1926	Mediterranean Palaearctica	Malaria important vector
48.	<i>maculipennis muscade</i> Fallenrod, 1926	European and Mediter- ranean Palaearctica	Malaria vector Romania.
49	<i>marginatus</i> (Banks, 1906)	Malayan Orient	Malaria suspected vector Philippines
50	<i>marshalli gibbatus</i> Evans, 1935	N and C. Trop. Ethiopia	Malaria minor im- portance.
51	<i>*melas</i> (Theobald, 1903) (= <i>pombiae</i> var <i>melas</i> Theo- bald, 1903)	N & C. Trop Ethiopia	Malaria important vector
52	<i>minimus</i> Theobald, 1901	Indian, Malayan and Chinese Orient	Malaria most im- portant vector foothills north India, Burma, South China.
53	<i>minimus flaviventris</i> (Ludlow 1914)	Malayan Orient	Malaria principal vector Philippines.
54	<i>monchei</i> Evans, 1925	N and C Trop Ethiopia	Malaria important vector some areas
55.	<i>monchei nigripennis</i> Evans, 1931	N Trop Ethiopia	Malaria important vector some areas.
56	<i>multicolor</i> Camboulin, 1902	Mediterranean Palaearctica	Malaria minor im- portance.
57	<i>neomaculipalpus</i> Curry 1931	C American, Andean and N Brazilian Neotropica (N)	Equine encephalitis experimental.
58.	<i>nili</i> (Theobald, 1904)	N and C. Trop. Ethiopia	Malaria important vector some areas.
59.	<i>noenabrosus</i> (Strickland, 1916)	Malayan Orient	Malaria vector Malaya.
60.	<i>oswaldi guayanaensis</i> Ratoon (= <i>larsimaculatus</i> of some authors)	N and S. Brazilian Neotropica	Malaria vector Brazil.
61	<i>oswaldi maculif</i> Galvão & Lane, 1937 (= <i>larsimaculatus</i> Root, 1923)	N and S Brazilian Neotropica	Malaria minor im- portance Brazil.
62.	<i>oswaldi nordestensis</i> Galvão & Lane 1937	N and S. Brazilian Neotropica	Malaria vector Brazil.
63.	<i>oswaldi oswaldi</i> Galvão & Lane, 1937 (= <i>larsimaculatus</i> <i>oswaldi</i> Peryassu, 1923)	C. American, Andean and N and S. Brazilian Neotropica	Malaria experi- mental, Brazil. Filariasis (N) bas- crofti experi- mental.
64	<i>pallidus</i> Theobald, 1901	Indian Orient	Malaria minor im- portance. Filariasis (W bas- crofti)

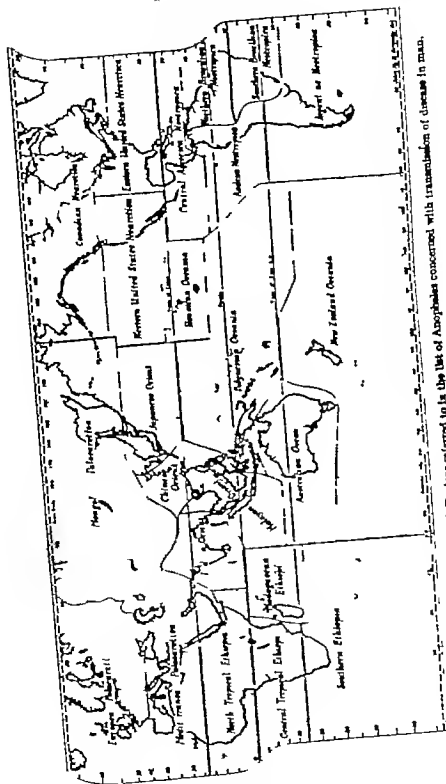
	<i>Species</i>	<i>Distribution</i>	<i>Disease</i>
65	<i>pattoni</i> Christophers 1928	Chinese Orient (N)	Malaria important vector China.
66.	<i>pharoensis</i> Theobald 1901	N & C. Trop Ethiopia S Ethiopia Medi- terranean Palae- arctica	Malaria important vector Upper Nile Province Sudan.
67	<i>philippinensis</i> Ludlow 1902	Indian and Malayan Orient	Malaria important vector Bengal. Filariasis (IV <i>ban crofti</i>)
68	<i>plumbeus</i> Stephens, 1928	European Palaeartica	Malaria doubtful importance
69	<i>pretoriensis</i> (Theobald 1901)	N and C. Trop. Ethiopia, S. Ethiopia	Malaria minor importance
70	<i>pseudopunctipennis</i> Theobald 1901	E. & W United States Palaeartica, Central American, Andean and N and S Brazilian Neotropica	Malaria, important vector some areas
71	<i>pulcherrimus</i> Theobald, 1902	Mediterranean and Mongolian Palaeartica, Indian Orient	Malaria minor importance.
72.	<i>punctimacula</i> Dyar & Knab 1906	C. American, Andean and N Brazilian Neotropica	Malaria important vector Panama.
73	* <i>punctulatus</i> Dönitz, 1901 (probably = <i>p. farauti</i> Laveran 1902)	Polynesian and Australian (N) Oceania	Malaria important vector New Guinea. Filariasis (IV <i>ban crofti</i>)
74	* <i>punctulatus farauti</i> Laveran, 1902 (= <i>p. moluccensis</i> (Swelengrebel and Sw de Graaf 1920)	Polynesian and Australian (N) Oceania	Malaria most important vector
75	* <i>quadrimaculatus</i> Say 1824	E. United States Neartica, C. American Neotropica	Malaria the most important vector United States.
76	<i>ramsayi</i> Covell, 1927 (= <i>pseudojamesi</i> Strickland & Chowdhury 1927)	Indian and Malayan Orient	Malaria minor importance. Filariasis (II <i>ban crofti</i>)
77	<i>rhodesiensis</i> Theobald 1901	N and C. Trop. Ethiopia, S. Ethiopia	Malaria minor importance. Filariasis (IV <i>ban crofti</i>)
78.	<i>rufipes</i> (Gough, 1910)	N and C. Trop Ethiopia, S Ethiopia	Malaria doubtful importance.
79	* <i>sacharovi</i> Favr 1903 (= <i>elutus</i> Edwards, 1921)	Mediterranean and Mongolian Palaeartica	Malaria important vector Balkans Palestine.
80	<i>separatus</i> (Leicester 1908)	Malayan Orient	Malaria minor importance.
81	<i>sergenti</i> (Theobald, 1907)	Mediterranean Palaeartica, Indian Orient (N W)	Malaria vector Egypt, Palestine.
82.	<i>smithi</i> Theobald, 1905	N Trop. Ethiopia	Malaria doubtful importance
83	<i>splendidus</i> Koidzumí 1920	Indian, Malayan and Chinese Orient	Malaria minor importance.

	Species	Distribution	Disease
84.	<i>squammosus</i> Theobald, 1901 ..	C. Trop. Ethiopia, Madagascan and S Ethiopia	Filaria (IV ben-crofti)
85	<i>stephensi</i> Liston, 1901	Mediterranean Palae- arctica (E.) and Indian Orient	Malaria important vector some urban, some rural areas. Filaria (IV ben- crofti)
86.	<i>stephensi mysorensis</i> Sweet & Rao, 1937	Indian Orient.	Malaria minor im- portance
87	<i>strodei</i> Root, 1928	C. American, Andean, N and S. Brazilian and Argentine Neo- tropica	Malaria doubtful importance.
88.	<i>subpictus</i> Grassi, 1899 (=rossi Giles, 1899)	Indian and Malayan Orient, Polynesian Oceania	Malaria important vector Celebes. Filaria (IV ben- crofti)
89	<i>subpictus malayensis</i> Hacker 1921	Malayan Orient	Malaria doubtful importance.
90	<i>sundaticus</i> (Rodenwaldt, 1928) (=hullows Theobald, 1903 var <i>sundaticus</i> Rodenwaldt, 1928)	Indian and Malayan Orient	Malaria important vector Bengal, Malaya, Indo- China, Nether- lands Indies. Filaria (IV ben- crofti).
91	* <i>superpictus</i> Grassi, 1899	Mediterranean Palae- arctica, Indian Orient (W)	Malaria important vector south Europe Middle East.
92.	<i>testellatus</i> Theobald, 1901	Indian and Malayan Orient	Malaria minor im- portance.
93.	<i>trianulatus</i> (Nerva & Pinto, 1923)	C. American, Andean, N Brazilian, S. Bra- zilian and Argentine Neotropica	Malaria suspected Venezuela. Filaria (IV ben- crofti) experi- mental.
94	<i>turkuali</i> Liston, 1901	Mediterranean Palae- arctica, N Trop Ethiopia (E.) Indian Orient	Malaria suspected vector.
95	<i>umbrosus</i> (Theobald, 1903)	Indian and Malayan Orient	Malaria important vector some areas.
96.	<i>vagus</i> Dönitz, 1902	Indian and Malayan Orient, Polynesian Oceania	Malaria minor im- portance India, Netherlands Indies.
97	<i>varus</i> Iyengar 1924	Indian Orient	Malaria important vector some areas, India, Burma. Filaria (IV ben- crofti)
98.	<i>restipennis</i> Dyar & Knab 1906	C. American and An- dean Neotropica	Malaria, minor im- portance, Hoo- dum.
99	<i>walkerii</i> Theobald, 1901	Canadian (S E.) and E. United States Ne- arctica	Malaria doubtful importance.

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(No references are given for the notorious anopheline vectors started with an asterisk, or for well known vectors of less importance)

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 80 *separatus* RUSSELL *et al* *ibid* p 121
 82. *smithi* RUSSELL *et al* *ibid* p 85
 86 *stephensi mysorensis* RUSSELL *et al* *ibid* p 122.
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Key to the Distribution Regions and Sub-Regions referred to in the list of *Anopheles* concerned with transmission of disease in man.

DISTRIBUTION REGIONS AND SUB-REGIONS.

PALAARCTIC REGION

- 1 European Palaearctica.
- 2 Mongolian Palaearctica.
- 3 Mediterranean Palaearctica.*

AUSTRALIAN REGION

12. Australian Oceania.
- 13 New Zealand Oceania.
- 14 Polynesian Oceania.
- 15 Hawaiian Oceania.

ETHIOPIAN REGION

- 4 North Tropical Ethiopia.
- 5 Central Tropical Ethiopia.
- 6 Southern Ethiopia.
- 7 Madagascan Ethiopia.

NEARCTIC REGION

- 18 Canadian Nearctica.
- 17 Eastern United States Nearctica.
- 18 Western United States Nearctica.

ORIENTAL REGION

- 8 Indian Orient.
- 9 Malayan Orient.
- 10 Chinese Orient.
- 11 Japanese Orient.

NEOTROPICAL REGION

- 19 Central American Neotropica.
- 20 Andean Neotropica.
- 21 Northern Brazilian Neotropica.
- 22 Southern Brazilian Neotropica.
- 23 Argentine Neotropica.

PENICILLIN

INDICATIONS FOR ITS USE AND METHODS OF ADMINISTRATION*

INDICATIONS.

1 The suitability of a case for treatment with penicillin depends not so much on the nature of the disease as on the susceptibility of the microorganism causing it some species are highly susceptible and others far too resistant for this treatment to have any effect. It follows that in diseases which may be caused by any of several different bacteria (e.g. meningitis, peritonitis) a bacteriological diagnosis is usually necessary if treatment is to be undertaken with any assurance of success

The chief organisms susceptible to penicillin are —

- Gonococcus.*
- Meningococcus.*
- Staphylococcus aureus*
- Streptococcus pyogenes*
- Streptococcus viridans* (most pathogenic strains)
- Pneumococcus.*
- C. diphtheriae*
- Clostridia* of gas-gangrene.
- Spirochaetes* of syphilis and relapsing fever possibly of Weil's disease.
- Actinomyces.*
- B. anthracis*

II *Penicillin* is indicated in the treatment of the following conditions when due to a susceptible organism unless the infection is likely to respond rapidly to sulphonamides —

- (a) Septicaemia (systemic administration)
- (b) Puerperal sepsis (systemic administration)
- (c) Acute cellulitis (systemic administration)
- (d) Acute osteomyelitis (systemic administration)

*Memorandum issued in March 1945 by the Ministry of Health and reprinted in full, by kind permission.

- (e) Cavernous and lateral sinus thrombosis (systemic administration)
- (f) Pneumonia (systemic administration)
- (g) Meningitis (intrathecal injection, often combined with systemic administration)
- (h) Carbuncles and acute abscess (systemic or local administration)
- (i) Certain types of empyemata (intrapleural injection)
- (j) Suppurative arthritis (intra-articular injection, sometimes combined with systemic administration)
- (k) Anthrax (systemic administration)
- (l) Actinomycosis (systemic administration)
- (m) Gonorrhoea, acute and chronic (systemic administration)
- (n) Gas gangrene and malignant oedema (systemic administration)
- (o) Other acute infections due to organisms sensitive to penicillin but resistant to sulphonamides.

III *Penicillin is often of value in the following conditions —*

- (a) Burns (cream or spray)
- (b) *Syccos barbae* (cream or spray)
- (c) Impetigo (cream or spray)
- (d) Dermatitis with infection (cream or spray)
- (e) Conjunctivitis and infections of cornea (eye drops cream or lamellae).
- (f) Infected wounds (powder cream, or in solution)
- (g) Encouraging results have recently been obtained in infections of the mouth and throat, using pastilles containing penicillin.
- (h) Penicillin may be used as a prophylactic agent in wounds exposed to infection.
- (i) Infections of the urinary tract due to sensitive organisms (systemic administration)

IV *Penicillin may be of value in the following diseases, but its place in relation to other forms of treatment has not yet been defined —*

- (a) Syphilis.
- (b) Subacute bacterial endocarditis.
- (c) Diphtheria.
- (d) Acute mastoiditis and otitis media.
- (e) Peritonitis.
- (f) Chronic osteomyelitis.

V *Penicillin is of doubtful value or of no value in the following conditions, for which it should not be used —*

- (a) Tuberculosis.
- (b) Acute rheumatic fever
- (c) Rheumatoid arthritis
- (d) Ulcerative colitis.
- (e) Infections caused by viruses such as influenza, anterior poliomyelitis and encephalitis lethargica.
- (f) All Gram-negative bacillary infections such as typhoid fever dysentery undulant fever and infections with *Bact. coli B* *influenzae* *Proteus* *Ps. pyocyaneus* and *Bact. Friedländer*
- (g) Glandular fever
- (h) Pemphigus.
- (i) Hodgkins disease and the reticuloses
- (j) Leukaemia.
- (k) Malaria.
- (l) Cancer

ADMINISTRATION

Unless the following properties of penicillin are appreciated unsatisfactory therapeutic results are likely to be obtained and wastage of this expensive drug is bound to occur —

(a) Once penicillin has been removed from the ampoule or tube it is likely to deteriorate, particularly if exposed to moisture or heat. Solutions or other preparations of penicillin exposed to air and kept at room temperature will not deteriorate significantly in 24 hours but should not be kept for more than 48 hours under these conditions.

(b) Penicillin is rapidly destroyed by boiling by most antiseptics and by enzymes of many of the common air bacteria.

(c) Penicillin should not be given by the mouth

(d) Penicillin passes rapidly from the blood into vascular tissues but the serous membranes and meninges present a barrier which penicillin does not readily penetrate.

(e) Penicillin is rapidly excreted in the urine for this reason it must be given at frequent intervals or continuously

(f) The diffusion of penicillin into dead or avascular tissues is slow. sequestra large sloughs or collections of pus are therefore likely to harbour bacteria out of reach of the drug and these usually have to be removed if treatment is to be effective.

I *Systemic administration* — Either the sodium or calcium salt may be used

(a) *Intramuscular injection* — 15 000 units dissolved in 2-3 cc. of sterile water or saline are injected every three hours throughout the day and night. This method is simple and effective but many patients find it difficult to tolerate on account of the pain produced.

(b) *Continuous infusion* by drip of 100 000 to 120 000 units daily into a muscle or vein. The drawback of the intravenous route is the high incidence of thrombosis otherwise this method is very satisfactory. The main drawback of the intramuscular route is discomfort and the development of local oedema when large amounts of fluid are given. This does not occur if special equipment delivering 100 cc. in 24 hours at a constant rate is used. The apparatus required is comparatively simple and this method of administration is preferred by many.

(c) *The duration of treatment* varies considerably according to the condition and response of the patient but should seldom be for less than five days or more than 12 days. Treatment is usually continued for about two days after a favourable response has been obtained.

(d) *The dosage* described above is recommended for all conditions requiring systemic treatment except the following —

(1) Syphilis 240 000 units daily for 10 days has been recommended.

(2) Gonorrhoea in uncomplicated cases a total of 100 000 units given in one day is usually effective.

(3) Bacterial endocarditis a daily dose of 240 000 units has been recommended but even prolonged treatment may be unsuccessful.

(4) Actinomycosis the dosage varies considerably according to the sensitivity of the actinomyces.

(e) *Toxic reactions*. — Pure penicillin will probably prove to be virtually non toxic, but penicillin as used at present contains impurities which occasionally give rise to minor reactions such as fever and urticarial rashes.

II *Local application*. — When applied locally penicillin must be brought into contact with the infecting organism. Merely to apply penicillin to the surface of an infection of considerable depth such as a boil or carbuncle is to waste time and penicillin.

(a) *Solutions* in sterile water or saline of 250 units or more per cc. are used for local treatment. The solutions may be used for injection through tubes stitched into wounds after closure or through a needle into *abscess cavities* after aspiration of pus. The injection should be made twice daily. Irrigation of an open wound is ineffective.

Burns of the face may be sprayed but penicillin creams are usually preferred for burns in other areas.

In *meningitis* a strength of 1,000 units per cc. is generally used, and from 5-10 cc. are usually injected daily by lumbar or external puncture. (The purer the penicillin the less likely it is to produce meningeal irritation)

In *empyema* 25 000 to 75 000 units in 50-100 cc. are injected every day or on alternate days, into the pleural cavity.

For *infections of the eye* drops of 500 to 2,000 units per cc. may be applied every half to two hours.

(b) *Powders*.—Penicillin (preferably the calcium salt) is mixed with sufficient sterile sulphathiazole or sulphathiazole powder to produce a final concentration of 2,000 to 5,000 units per gram. The powder can be blown with an insufflator on to raw surfaces or into wounds, and the application should be repeated once or twice daily.

(c) *Creams*—Several types of cream have been recommended, but the following is satisfactory for most purposes—

The base consists of 30 per cent lanette wax SX in water. The requisite amounts of lanette wax and water are heated to 40°C. The water is slowly mixed into the wax in a mortar and stirring is continued until the mixture is almost cold. This usually takes about ten minutes, when a smooth cream is formed. The emulsion is then autoclaved at 20 lbs. pressure for 20 minutes. When it has cooled to about 40°C. the correct amount of penicillin, dissolved in a few cc. of sterile distilled water is added and thoroughly mixed with a sterile rod or spatula.

The cream is usually applied daily.

III. Further instructions regarding the use of penicillin in the treatment of V.D. are in course of preparation, and will be issued in due course to all V.D. authorities.

SUMMARY OF RECENT ABSTRACTS.*

VI. PLAGUE.

Epidemiology

TRUFANT (p. 481) in a general account of sylvatic plague in the United States, states that reservoirs of infection have been proved in more than 31 rodents and in rabbits. In *Public Health Reports* Washington (p. 36) a statement is made of the incidence of plague in the United States during 1942. There was one human case and infection in rodents or their ectoparasites was detected in six western States.

It has not been very clear how plague is carried over in a rodent population from season to season, but in an investigation of plague in ground squirrels in

*The information from which this series of summaries has been compiled is given in the abstracts which has appeared in the *Tropical Diseases Bulletin* 1944 v. 41. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

California MEYER *et al* (p 398) have now established the fact that latent disease occurs in these animals. In this form of plague there are no inflammatory or encapsulated lesions but the bacilli persist in the tissues and have been found in 15 of 90 pools of pulped spleen liver and lymph glands from 440 animals. The authors point out that estimation of plague in field rodents by examination for visible lesions is futile because such examinations cannot detect this latent plague. It is thought that bacteraemia may develop in latent plague and permit the infection of ectoparasites.

SÁENZ VERA (p 481) reports that proof has been obtained of Macchuiavello's finding that fleas inhabiting the nests of rats can preserve a plague infection for a long time and that for this reason plague though absent from the animal population for several months may reappear later. This fact is important in any plan for control. Nests and burrows can satisfactorily be destroyed by cyanogas or flame-throwing bombs. The author notes that guinea-pigs or cubs are often responsible for epizootics and that these animals are rather domestic than sylvatic in habit.

In discussing sylvatic plague in the province of Córdoba Argentina DE VILLAFARÉ LASTRA *et al* (p 393) point out that the disease exists in the rodents of the forest and agricultural regions of the north and that it is at present uncontrollable forming a permanent focus which may become a menace to the urban centres.

KAMAL and his colleagues (p 566) discuss plague in Egypt where the disease is endemic but where epidemic outbreaks occur from time to time. In their opinion the accepted incubation period (6 days) is too short since they have seen cases arising on the 13th day in contacts left in their homes. [An explanation of this may perhaps be transmission by *Pulex irritans* as suggested by Blanc and Baltazard below.]

TOWNSEND (p 480) notes that plague is reported every year in Port Said and though the numbers of cases are usually small the disease might become epidemic. In 1942 pneumonic plague was reported for the first time and nine cases occurred in a month. At first the correct diagnosis was not made. Treatment with sulphapyridine was not successful in either bubonic or pneumonic cases.

METZNER (p. 490) has published an account of the development and spread of plague in Africa.

Transmission

Plague is usually transmitted from rat to man by rat fleas but transmission from man to man by *Pulex irritans* [though it has certainly been postulated] is not generally considered important. BLANC and BALTAZARD (p 281) were attracted to this possibility when they observed the frequent occurrence of successive cases in individual families during an outbreak of plague in Morocco. They collected *P. irritans* from persons who had died of plague and from the rooms they had occupied and from these collections isolated 29 strains of *P. pestis* by animal inoculation. The organism was transmitted to clean fleas allowed to feed on a patient and was found to persist for 21 days in fleas from infected houses. Animals were infected by the bite of fleas taken from the houses of dead persons.

ROUBAUD and GIRARD (p 567) give reasons for thinking that *Paractenopsyllus kerghuelis* and *Synopsyllus fonquernis* which infest many species of mammals in the forest region of Madagascar may be important in the spread of sylvatic plague.

PRINCE (p 37) notes that the fleas *Opisocrostis tuberculatus tuberculatus* *O. labris* and *Oropsylla rufipes* have been proved possible vectors of plague. He has now demonstrated that *Opisocrostis bruneri* and *Thraassis bacchi* are effective

transmitters after feeding upon infective animals that they are in fact, as effective as the well-known species *Xenopsylla cheopis* and *Diarmatops montana*. All these fleas have been found on rodents in the United States, and there is a continuous chain of possible hosts and vectors from the Rocky Mountains to the States east of the Mississippi—hence the danger of spread of sylvatic plague to the hitherto uninfected eastern States.

BURROUGHS (p. 666) has succeeded in transmitting plague experimentally by the flea *Ualareus telchinus*.

HECHT (p. 1034) in a study of a small outbreak of human plague in Venezuela, relates it to the presence of *Xenopsylla brasiliensis* among the *Rhopalosiphum* fleas captured on sylvatic rodents, in which the disease was present. He thinks that in field studies, not only the flea index, but also a count of species of fleas should be made so that the prevalence of known plague vectors can be assessed.

Actiology

GIRARD (p. 38) argues that the plague and pseudotuberculosis organisms should not be included in the *Pasteurella* group—he now quotes experiments which showed that these organisms may be sensitive to phages of the dysentery group. Nevertheless, this fact does not justify any contention that the organisms of plague and dysentery have antigenic characters in common. In a discussion of this view BLANC agreed that the lytic principle of the plague bacillus could not be transferred to the *Pasteurellas* and said that the latter instead of multiplying in *Xenopsylla cheopis* were destroyed in 24 hours. He therefore agreed with Girard.

MACCHIARELLO and PARACAMPOS [this Bulletin 1943 v 40 49] have already shown that *P. pestis* can survive for 284 days on solid media kept at laboratory temperature. FRANCIS (p. 214) now reports that viable bacilli were recovered from cultures on beef infusion agar which had been kept at 10°C. for 24 years. Some of the animals injected with these cultures after that period of time died of acute plague others died but without the signs of plague others survived.

SOKLEY and HANBU (p. 129) after careful tests under strictly controlled conditions have found the optimum temperature for the growth of *Pasteurella pestis* in broth to be 27°–28°C. At this temperature growth was about five times as abundant as at 37°C. Limiting temperatures are –2°C. and 45°C. The same authors (p. 129) have found that growth is optimum at pH 7.2–7.6 and fairly good between 6.6 and 8.0. Buffering of the broth medium greatly reduced the growth.

DEVICAT (p. 668) had previously found that continuous aeration of the culture medium resulted in loss of virulence of *P. pestis* growing in it. In repeating the experiment he used quacklime instead of caustic potash to treat the air before bubbling it through the culture, and failed to reduce the virulence. He now thinks that the reduction which originally occurred was due to radio-activity of beta emanation from the caustic potash, and that this was not present when lime was used. By using hydrogen washed in caustic potash in much the same way he has obtained a non-toxic strain of *Clostridium triarii*.

McMAHON (p. 753) has shown that, although natural infection has been reported in the hamster (*Cricetus cricetus*) the golden hamster (*Mesocricetus auratus*) is highly resistant to plague, in comparison with other test animals, and is not suitable for routine test experiments.

Vaccination Control

The Director of the Haffkine Institute (p. 38) states that the research under taken there has confirmed the greater protective power of living avirulent immunogenic vaccine over killed vaccine. A method has now been found of

reducing at will the virulence of a strain and the immunogenic power can be measured during the process of attenuation. Suitable strains can therefore be chosen as desired for the preparation of live vaccine. It is probable that continued subculture will cause strains to lose their immunogenic power altogether. The killing of cultures by methods so far used greatly reduces their immunogenic power.

JAWETZ and MEYER (p. 400) believe that properly tested live vaccines are safe and better in immunogenic power for experimental animals than any killed preparations now in use. The vaccines must be composed of avirulent organisms (i.e. unable to cause death of an animal unless introduced in sufficient quantity to cause toxic death without multiplication) and it is necessary that the strain be developed from a single cell. If this is done there is no danger of reversion to virulence. Avirulent strains may be produced by growth of virulent strains in alcohol broth at high temperature, by isolation of single colonies and prolonged incubation in broth at 32°C. or by passage through immune animals. The authors point out that the antigenic constituents of importance in immunization may differ in their resistance to heat and that strains are protective in different degrees to different animals.

The same authors (p. 753) make it clear that although there is strong support for the use of live avirulent vaccines rather than of dead organisms it is not every avirulent organism which is immunogenic. The immunogenic activity of a strain cannot be correlated with invasiveness or survival in the body and must depend on antigenic constitution because strains are distributed equally and persist for the same length of time in different host animals yet immunogenic activity is different for these animals. The distribution of virulent and avirulent strains differs only quantitatively in the animals. Large toxic doses of avirulent organisms produce a cumulative mortality curve which closely resembles that found after injection of small doses of virulent bacilli.

These same workers (p. 847) note that loss of virulence of *P. pestis* is to some extent selective for the species of test animal used. At one time it was suggested that possession of an envelope was a factor in determining virulence [see this *Bulletin* 1941 v 38 327] but the authors do not accept this view and state that investigation into antigenic constitution has not solved the problem. The most striking character which serves to differentiate virulent from avirulent organisms is the inability of the latter to proliferate freely even in susceptible experimental animals. [In the original abstract this inability to proliferate was wrongly given as a character of virulent organisms.] Chick embryos are highly susceptible to plague and are killed in four to eight days by 20 virulent or 200 000 avirulent *P. pestis*. In small dose the avirulent organisms fail to proliferate in the organs the virulent organisms do so. The susceptibility exhibited by chick embryos is attributed to absence of cellular defence mechanism. Hyperimmune serum does not protect them which indicates that a cellular mechanism must be present for antiserum to exert its protective action.

PORGES (p. 482) has demonstrated that rats are able to burrow under walls 48 inches below the surface but that a sure protection of buildings is afforded by curtain walls to a depth of 24 inches provided that at the bottom of these walls there is a horizontal flange projecting 8 inches.

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DE VILLAFANE LASTRA and RODEIRO (p. 399) describe plague meningitis in four cases of bubonic plague. In all the cerebrospinal fluid was turbid and contained the bacilli. As these cases were found in a series of 39 hospital admissions for plague in whom the cerebrospinal fluid was examined the authors believe that meningitis would be found more often than hitherto if a systematic investigation of the nervous system were made in all cases.

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SOKNEY and WAGLE (p. 37) in a field study of the treatment of plague have reached the conclusion that the most important single factor which influences the result of treatment is the occurrence and degree of septicaemia. Without septicaemia spontaneous recovery is usual but with septicaemia this is not so. Mild septicaemia is that in which less than 10 colonies develop from 0.25 cc. of blood severe septicaemia is that in which more than 10 appear. In the series of cases considered no selection was practised except that patients who died within 24 hours are excluded and treatment was given with serum, sulphathiazole, sulphapyridine, sulphathiazole with serum, or (as controls) with intravenous iodine. For all cases the death rates with the first four of these treatments varied from 20 to 27 per cent. with iodine it was 53.6 per cent. for septicaemic cases only the rates were from 38.1 per cent. (sulphathiazole with serum) to 72.2 per cent. for the first four groups with iodine the rate was 96.4 per cent. The doses of the sulphonamides were—sulphathiazole 10 gm. the first day and 7.5 gm. daily for 4–5 days (blood concentration 5–10 mgm. per cent.) sulphapyridine 8 gm. the first day and 3–4 gm. daily for four days (concentration 5–10 mgm. per cent.) Treatment did not save any of the 10 pneumonic cases which were not included in the figures given above.

The Director of the Haffkine Institute (p. 38) reports that the efficacy of sulphathiazole seems to be evident and that a marked advantage was noted when serum and sulphathiazole treatments were combined.

HALLAT (p. 940) reports on the results of sulphonamide treatment of plague in India. Sulphapyridine and sulphathiazole were used, in doses of $7\frac{1}{2}$ gm. the first day 4 gm. daily on the 2nd and 3rd days, 3 gm. daily on the 4th–6th days. The results were somewhat disappointing, with a case mortality rate of 42 per cent. but this was probably due to the fact that in many cases treatment was late.

DE VILLAFANE LASTRA *et al.* (p. 400) have experienced very good results in the treatment of plague (the diagnosis having been confirmed bacteriologically) with sulphathiazole in spite of earlier failure with sulphanilamide and sulphapyridine. Sulphathiazole should be given early and in high dosage (10 gm. daily for an adult to maintain a blood concentration of 8 mgm. per cent. or more) and should be continued until cure is effected unless there is manifest intolerance of the drug. The authors have no faith in serum treatment.

JAWETZ and MEYER (p. 1034) state that the treatment of choice is obtained by the use of hyperimmune serum in combination with chemotherapy. Hyperimmune serum was obtained from rabbits given three intravenous injections of living avirulent *P. pestis* on alternate days. In this serum there was no correlation between the antitoxic and the antibacterial power—a detectable level of antitoxic substances is attained only if a re-stimulating injection is given 3–4 weeks after the primary series of injections. A mouse test is described for the assay of anti-infectious and antitoxic substances in such sera.

The same authors (p. 1035) note that plague antiserum is weak in comparison with other antisera. In a study of immunity in plague they emphasize opsonic activity. Whole blood of immune animals can destroy a much greater number of plague bacilli than blood of normal animals—the activity seems to be inherent in the plasma not in the cells. Immune animals are able to fix the bulk of infected *P. pestis* at the site of injection but fixation does not involve lymphatic blockage. Splenectomy does not reduce resistance to plague. They also note that extracts of both virulent and avirulent plague strains contain a spreading factor.

KAMAL *et al.* (p. 596) advocate combined treatment with serum (not less than 80 cc.) and sulphapyridine (2 gm. on admission followed by 1 gm. in two hours and then 1 gm. every four hours). For rat control they use a local preparation of *Urginea (Scilla) maritima*.

WAYSON and McMAHON (p 848) have used sulphadiazine in the treatment of guinea-pigs infected with plague the results indicate that there may be value in the treatment of human disease by this drug in the stage before the development of bacteraemia.

Charles Wilcocks

MALARIA.

GUTSEVICH A. V. On the Mosquitoes of North Iran. *C R Acad Sci URSS* Moscow 1943 v 40 No 3 123-5 [Summary taken from *Rev Applied Entom.* Ser B 1945 Feb v 33 Pt. 2, 16]

A list is given of mosquitos found in northern Persia in May-July 1942, showing their abundance in two provinces on the Caspian coast and two on the Iranian plateau. The species of *Anopheles* taken were *A. maculipennis* Mg., *A. superpictus* Grassi, *A. hyrcanus* Pall. *A. claviger* Mg (*bifurcatus* auct.) *A. algeriensis* Theo *A. plumbeus* Steph and *A. pulcherrimus* Theo *A. maculipennis* was very abundant and associated with severe malaria in the humid Caspian provinces where it bred in the numerous rice-fields. Examination of eggs showed that it was represented by two varieties in these provinces of which one was var *sacharovi* Favt. It occurred in small numbers only in the much less malarious plateau provinces which are at an altitude of over 3 000 ft and are characterised by a dry climate scarcity of water and poor vegetation. Of the other *Anophelines* the only one considered of any importance in relation to malaria is *A. superpictus*. It was found in two districts both on the plateau but does not become abundant until late summer and autumn.

PAMPANA, E. J. L'immunité anti paludéenne et son rôle dans l'épidémiologie [Malarial Immunity and its Role in Epidemiology] *Acta Tropica* Basel. 1944 v 1 219-30

RUSS S E. & GAYNOR, J S Spontaneous Rupture of a Malarial Spleen. *J Amer Med Ass* 1945 Mar 31 v 127 No. 13 758.

TEMKIN O & RAMSEY Elizabeth M. Antimalarial Drugs. General Outline 110 pp [Bibliography] National Research Council. Division of Medical Sciences. Issued by the Office of Medical Information (Under grants of the Carnegie Corporation and the Johnson & Johnson Research Foundation.) Washington 1944 March.

The war in the Pacific compelled careful revision of our methods for controlling malaria and the loss of Java and its quinine supplies necessitated the overhauling of our choice and use of antimalarial drugs. The present volume is a careful review of the information available in the published literature about such compounds and it has been compiled as a basis for the revision which the military situation demanded.

The first part of the work describes the quinine situation in war time the principles on which the antimalarial compounds pamaquin (plasmoquine) and mepacrine (atebrin) were discovered, and the general pre-war opinions about antimalarial drugs are set out in the Third and Fourth General Reports of the Malaria Commission of the Health Organisation of the League of Nations issued in 1933 and 1937 respectively. A list is included based on the review by CURD [this *Bulletin* 1944 v 41 101] of the main compounds studied during the pre-war years with indications of their action upon avian simian and human

malaria. Detailed summaries are given of the literature concerning the pharmacology antimalarial activity and toxicology of quinine mepacrine and pamaquin. These summaries should prove valuable to the investigators who are now engaged in studying the use of these compounds under war conditions and it is mainly for them that this work has been compiled but to the general student they would prove misleading on many points for they omit all the newly acquired information which is now restricted to confidential reports and which considerably modifies pre-war views in many particulars. Similarly the section on "Treatment Plans of Malaria under Present War Conditions" is more valuable as history than as a guide to immediate conduct. This section does not reach any conclusion as to the relative merits of quinine and mepacrine as will be remembered, recent statements by the American Board for the Coordination of Malarial Studies and by the Malaria Committee of the British Medical Research Council [this *Bulletin* 1945 v 42, 89] declared that mepacrine was in all respects as satisfactory as quinine and in many respects it was better especially in its greater power to suppress and to cure malignant tertian malaria. Similarly the section reviewing the action of sulphonamides on malaria can do little more than indicate that these compounds have potentialities which are worth investigating. Limiting itself to published literature it cannot go on to say that they have now been investigated and have not been adopted for current use.

Subsequent sections deal with other compounds such as thio-bismol, which show minor degrees of antimalarial action. Nowadays when new means are being sought to produce radical cure of malarial malaria the summary of information about neoraphenamine is timely. The antimalarial action of this compound is limited to *P. vivax* and it does not extend to *P. falciparum* and even with vivax malaria, although neoraphenamine will usually cut short the immediate attack, most reports agree that it is no more effective than quinine or mepacrine in preventing subsequent relapses. Antimonials mercurials, amidino compounds and derivatives have all been reported to show antimalarial action under certain conditions, but in no case have the facts suggested that these compounds would be valuable for general clinical use.

To sum up this review is valuable to the persons for whom it was designed, viz., those now engaged in wartime research on antimalarial compounds but it would be misleading in many respects to readers who have not access to American and British confidential information.

F. Hawking

- I. ANDREWS J C & CORNATEER W E The Effect of Acid and Alkali on the Absorption and Metabolism of Quinine. *J Pharm & Exper Therap* 1944 Nov v 82, No 3 281-5
- II. — & — The Absorption of Quinine Salts from Isolated Intestinal Loops of Dogs. *J National Malaria Soc. Tallahassee, Fla.* 1944 Dec., v 3 No. 4 231-6.

I. HAAG *et al* (*J Pharm & Exper Therap* 1943 v 79 136) found in human subjects that the extent of urinary elimination of quinine given orally in a single dose was related to the pH of the urine. The smaller elimination in alkaline urine was assumed to be due to greater resorption of quinine from the urinary tract. Previously ACTON and CHOPRA and later SIKTOR [this *Bulletin* 1925 v 22, 814 1931 v 23 596] had recommended the giving of alkali with quinine on clinical grounds. The results of GUILLOTROYA-GURYEA [*Klinicheskaya Meditsina* 1936, v 16 386] [not available to the reviewer] apparently imply that alkali delays the onset of urinary excretion of quinine without affecting the total amount excreted. The present authors in seeking an explanation of the mechanism of these reactions, have investigated the rate and degree of absorption

of quinine from the intestinal tract under varied conditions of pH. In this connexion they have also considered the acid base balance of the body as a whole as well as its effect on the degree of metabolic decomposition of quinine and therefore on the amount of unchanged drug excreted. The influence of the pH of urine on the keeping qualities of quinine excreted in it was found to be negligible when the urine was protected from light.

Isolated loops of the small intestine of dogs (described below) were used in the absorption studies. Two lines of investigation were followed. In the first the acid or basic agents were given along with quinine in the intestinal loops and in the second they were administered orally while the quinine salt in solution or suspension was given as before. The effect on the speed of absorption of adding equivalent amounts of alkali to either quinine dihydrochloride or sulphate in the loop will be reported later. The standard doses of quinine corresponded to 20 mgm. of the anhydrous sulphate per kgm. of body weight. When 0.5 gm. of ammonium chloride giving a pH of about 5 was used in the loop no evidence was obtained of increased rate of absorption and the higher urinary excretion under acid conditions was left unexplained. The effect of oral ingestion of sodium bicarbonate or ammonium chloride or benzoate for two days before quinine was added to the loop and for two days afterwards (by which time practically all quinine excretion is ended) on the rate of absorption and the percentage of the absorbed dose excreted in 48 hours was next investigated. The absorption period was 60 minutes and control animals received quinine alone. Urine was collected by catheter at the appropriate times and the total volume voided was known. A urinary pH as low as 6.0 was not attained. Relatively small amounts of quinine were excreted during the second 24-hour period. Based on the amount absorbed there was no evidence that alkali therapy delayed significantly the excretion of quinine. The lowered percentage excretion of this substance during alkali administration as noted by other authors was confirmed but the results were not explained by differences in absorption following administration of acid or alkali.

ii This paper deals with the rate and degree of absorption of therapeutic agents from the intestinal tract and the methods employed in studying them. When such absorption is correlated with blood levels and urinary excretion, it is not always certain that changes in the parent substance as a result of metabolic processes in the organism are taken into account in the methods of estimation employed. In the case of quinine for example the methods of estimation lack specificity. When absorption is considered for the whole intestinal tract, only a single experiment is possible with each animal. The present authors use in dogs an isolated intestinal loop about 1 foot long from the jejunal region. The distal end of the loop whose blood and nerve supply is preserved intact is closed and the proximal end is brought to an opening in the abdominal wall and the remaining ends of the intestine are anastomosed. The method allows of repeated experiment with the same animal as the dogs may exist on normal diet for several years. The substance whose absorption is to be investigated is placed in the loop which can be washed out at the appropriate time and there is no faecal loss. The absorptive surface is limited in extent, and may lose its absorptive power after a time. It was found however that blood levels of quinine attained by this method were the same as in normal animals. Comparison has been made of the rates of absorption of quinine base and its salts. It was found that in the early stages the more soluble dihydrochloride was absorbed more rapidly than the sulphate but differences in the rates of absorption decreased with time. In a 30 minutes experiment the rate of absorption of quinine base was greater than that of the sulphate. Mention is made of the results obtained in the above paper and figures are given for the rates of absorption of salts of other alkaloids of the cinchona group. J. D. Fulton

HAWKING F. Local Effects of Intramuscular Injection of Solvochin. *Brit Med J* 1945 Mar 24 412.

Solvochin is a soluble preparation of quinine with antipyrin ampoules of 2.2 cc. containing $7\frac{1}{2}$ grains of quinine base [see this *Bulletin* 1945 v 42, 177] and it is said to be painless when injected intramuscularly. The author investigated its action on the tissues at the site of injection for comparison with the action of mepacrine and quinine dihydrochloride observed in previous similar experiments [see this *Bulletin* 1943 v 40 823, 1944 v 41 1005].

The solution supplied in ampoules was diluted with sterile isotonic saline (1 cc. diluted to 7.5 cc.) so that 0.5 cc. contained 16 mgm. of quinine base corresponding to 20 mgm. of quinine dihydrochloride in 0.5 cc. which was injected in the previous experiments. Injections were made into the muscle of the loin and thigh of rabbits and also into the subcutaneous tissue of the abdominal wall. Control injections of normal saline produced no local injury. The rabbits were killed after 1 to 8 days and their tissues examined.

Macroscopical—The loin muscle showed a necrotic mass about $3 \times 0.9 \times 0.6$ cm. in size, surrounded by a narrow yellow zone of leucocytic reaction. In the thigh muscles the effects were more varied—a necrotic mass in some cases in others small punctate haemorrhages or a whitish roughened appearance of the surface of the muscles. In the thigh the injection is largely distributed between the muscles whereas in the loin it is chiefly retained within the muscle.

Microscopical—Sections of the loin muscle showed necrosis and leucocytic reaction. On the first day after injection there were many polymorphonuclear leucocytes with, sometimes, fibrinous fluid, but after 5 to 8 days, most of the leucocytes were mononuclear, and granulation tissue with fibroblasts was present. After eight days some of the necrotic muscle fibres were becoming calcified. In the thigh muscles the necrosis varied in amount, there was a slight infiltration of leucocytes and a moderate distension with fluid was present. In the skin some necrosis of the subcutaneous layer of muscle was found and the adjacent connective tissue showed a little fluid and a few small round cells.

The lesions were indistinguishable in character and extent from those caused by the injection of a corresponding amount of quinine dihydrochloride.

J. F. Corson.

McCONNIS J. H. Hippuric Acid Liver Function Test in relation to Malaria and Atabrin. *U.S. Nav Med Bull* 1944 Dec v 43 No. 6 1163-5

The patients had been stationed in a highly malarious area in the South-West Pacific and had taken mepacrine 0.9 gm. weekly for at least four months prior to the examination. From the large number of patients available fifty-five were selected on account of their severe symptoms e.g. prolonged fever delirium, vomiting and diarrhoea. The patients had also received a standard course of quinine, mepacrine and pamaquin and all but two had had two or more intensive courses of mepacrine. They were given a standard course of quinine sulphate 2 gm. daily for three days and mepacrine 0.3 gm. daily for five days. On the second or third day with mepacrine the patients were given 6 gm. sodium benzoate by mouth and the four-hour yield in urine was measured. All except eight of the patients showed a yield equivalent to 3 gm. or more sodium benzoate which was taken as the level of normality. Five of those giving abnormal responses had icteric sclerae. One was obviously jaundiced, one gave a similar low response when the test was repeated four days later and the other six gave normal responses when tested on the twelfth day of treatment. It was considered that the cause of the lowered liver tolerance was the malarial attack itself, since the normal condition was regained in a few days although the patient

was still taking large doses of mepacrine. In an appendix the author states that in the year since this paper was written the dose of suppressive mepacrine has been increased to 0.5 gm. twice weekly. No evidence of liver damage has been observed and the incidence of malaria has been diminished. [Elaborate investigations carried out at military centres in Britain have shown that long continued administration of mepacrine 0.1 gm. daily has no harmful effect upon the liver or kidney as evidenced by organ function tests.]

F. Hawking

SCHOOF, H. F. Adult Observation Stations to determine Effectiveness of the Control of *Anopheles quadrimaculatus*. *J. Econom. Entom.* 1944 Dec v 37 No 6 770-79 1 fig.

This useful paper is in the form of a discussion the purpose of which is to list and consider comparatively the various types of adult anopheline catching stations and their organization as used during the past four years in the Malaria Control Programme in North Carolina. The subject is considered under the headings of baited and non baited stations although as the author points out the two are not always clearly distinguishable. — In practice it should be kept in mind that a non-baited shelter such as an anopheline house if placed adjacent to a pig sty is for all entomological purposes an animal shelter. For various reasons human habitations proved unsatisfactory as a means of judging anopheline density in baited shelters and recourse was had to shelters housing cows horses pigs or goats. Chicken houses were less productive than animal shelters. Non-baited stations include such natural resting places as culverts bridges and hollow trees but the most useful results were obtained by the use of non baited anopheline houses. These are wooden shelters 3x3x6 feet built of scrap lumber and consisting of four sides with an overlapping roof the structure being fastened together with hooks. Such houses are easily transported and can be erected at the selected site within ten minutes of arrival. The value of light traps is discussed and Schoof considers that their chief use is in urban areas or military posts where animal sheds are not available. The paper contains much valuable information which does not lend itself to summarization, and the article should be consulted in the original by those interested.

R. M. Gordon

ROSE, G. Fortschritte in der Bekämpfung des Läuse-Fleckfiebers und der Malaria. [Improvements in the Control of Typhus and Malaria.] *Acta Tropica*, Basel. 1944 v 1 193-218

In this paper reference is made to experiments on the action of DDT on lice and mosquitoes. The author writes from the Robert Koch Institute Berlin.

DAS GUPTA, B. M. & SIDDONS, L. B. Treatment of Simian Malaria (*P. knowlesi*) with Stilbamidine—M & B 744. *Indian Med. Gaz.* 1944 Nov v 79 No 11 527-8

Infection with *Plasmodium knowlesi* in rhesus monkeys is practically always fatal but the infection can be controlled by atabrin or quinine. In the case of the former however there is a relapse rate of about 100 per cent even after five days intensive treatment or more prolonged treatment with small doses. After quinine the relapse rate is only 18.7 per cent. In both cases the relapses may be as severe and fatal as the primary attacks. Trials with stilbamidine reported in this paper show that 16 of 20 monkeys survived the primary infection. The drug was administered intravenously each day in doses varying with the weight.

of the animal. The days of treatment varied from 1 to 8 and the dose of drug from 0.001 to 0.0175 gm. (0.001 to 0.005 gm. per kgm. of body weight). There was evidence that the parasites underwent degeneration during treatment. In eight of the animals which received doses of 0.002 gm. or more per kgm. of body weight only one relapsed.
C. M. Wexon.

HUFF C. G. & COULSTON F. The Development of *Plasmodium gallinaceum* from Sporozoite to Erythrocytic Trophozoite. *J. Infect. Dis.* 1944 Nov-Dec. v 75 No 3 231-49 64 coloured figs. on 2 pls. [Numerous refs.]

The authors give the first complete account of the development of a malarial parasite between the injected sporozoite and the first appearance of parasites in the red blood corpuscles. This development takes place in the cells of the reticulo-endothelial system in which it has been studied by the authors in young chickens inoculated with sporozoites of *Plasmodium gallinaceum* from the salivary glands of infected *Aedes aegypti*. The technique adopted was to inoculate large numbers of sporozoites into a limited area of the skin of the wing. Areas of this kind were removed after desired intervals fixed sectioned, and suitably stained. By examination of the sections it has been possible to follow the whole development. In addition, intravenous inoculations were carried out with a view to the study of development in the internal organs.

Thirty minutes after the injection of the sporozoites into the skin they are detectable in the intercellular spaces and on the surface of the cells. A few may be seen at this stage bent or coiled within vacuoles in the cytoplasm of the macrophages. After the expiry of six hours sporozoites are no longer found in the intercellular spaces. Instead, oval or spheroidal parasites evidently the result of rounding off of the sporozoites are seen in the macrophages. From the 6th to the 17th hour there is little change in these forms apart from a slight increase in size. From the 18th to the 24th hour there is a further growth, and the single nucleus becomes double. After the 24th hour there is rapid growth and the nucleus increase to over 100. The mature schizonts or segmenters make their appearance from the 36th to the 48th hour. These consist of a central core to which the merozoites are attached in a radial manner. The appearance is reminiscent of the sporozoites within the mature oöcyts on the mosquito's stomach. The whole of the development from the sporozoite to the mature schizont is termed by the authors the cryptozoc generation and the parasites themselves cryptozoites. The merozoites are cryptozoc merozoites. It is suggested that the core as it is called, to which the merozoites are attached, may after liberation of the merozoites produce a further brood of merozoites. (It seems to the reviewer however that the core most probably represents the residual body which is commonly associated with the production of merozoites and sporozoites amongst the sporozoa.)

When the cryptozoc merozoites are liberated they enter other macrophages in the skin or as it appears wander further afield and enter cells of this type in other situations. These merozoites become rounded, as did the sporozoites in the first place and develop in the same manner finally producing mature schizonts with merozoites at about the 75th hour. The second generation, as indeed all subsequent generations of exoerythrocytic forms to distinguish them from the first or cryptozoc generation are given the name metacryptozoc, the parasites of these generations being termed metacryptozoites. The majority of the metacryptozoc merozoites enter other macrophages, either locally in the skin or in more remote organs but some appear to enter the erythrocytes as a few parasites have been seen in the blood as early as the 75th hour after the intravenous injection of a heavy dose of sporozoites. After the completion of the

first metacryptozoic cycle the second metacryptozoic cycle commences but the development now proceeds less regularly while practically all organs become infected.

At about the fifth day another type of schizont begins to appear. This gives rise to a large number (500-1 000) of small micro-merozoites in contrast to the earlier schizonts with a small number (100-200) of larger macro-merozoites. In animals inoculated intravenously with large numbers of sporozoites cryptozoites are found only in small numbers in the organs. Later however meta cryptozoites appear in the organs in abundance. As regards the appearance of parasites in the erythrocytes the earliest was at the 75th hour. With smaller doses of sporozoites the interval is extended till after the bite of a single infected mosquito erythrocytic parasites are not found till the 7th to 10th day. These differences may be due not to the later appearance of erythrocytic forms but to the fact that with smaller doses of sporozoites they are increasingly difficult to find. After the intravenous injection of sporozoites during a 24-hour period at about the sixth seventh or eighth day there is a sudden 200-fold increase of erythrocytic forms above the number in the preceding 24-hour period. At this period large numbers of metacryptozoites producing micromerozoites are to be found in the internal organs and appear to have a relationship to the sudden flooding of the blood with erythrocytic parasites.

As a control of the results obtained by the injection of sporozoites attempts were made to follow the development after actual mosquito bites. It was found that sporozoites injected by the mosquito were able to develop locally in the skin as well as in the more remote organs. There was an exact parallel to the development following intradermal subcutaneous or intravenous inoculations of sporozoites.

The authors point out finally that the only species of malarial parasites in which cryptozoites have been found are those in which abundant exoerythrocytic stages occur. There is a danger in assuming that all species of *Plasmodium* must have a similar development though there is much indirect evidence against the view that a sporozoite is capable of directly invading a red blood corpuscle.

In the discussion to the paper the authors examine the earlier work of MISSIROLI (1933-1941) KIKUTH and MUDROW (1939-1940) SCHULEMANN and SPIES (1940) and REICHENOW and MUDROW (1943) [this *Bulletin* 1935 v 32 795 1938 v 35 569 1940 v 37 671 1941 v 38 294 1942 v 39 123 399 1944 v 41 190] on the development of sporozoites. The conclusion is that the work of some of these observers has added fragmentary knowledge of the life-cycles of the malarial parasites with which they worked but in no case has the complete cycle been elucidated.

The paper is illustrated by two excellent coloured plates which depict clearly in 64 figures the various developmental forms described. C. M. Wenyon

HAAS V. H. & EWING FRANCES M. Inoculation of Chick Embryos with Sporozoites of *Plasmodium gallinaceum* by inducing Mosquitoes to feed through Shell Membrane. *Pub Health Rep* Wash. 1945 Feb 16 v 60 No 7 185-8 1 fig. on pl.

Fertile hens' eggs which have been incubated for 10-13 days are exposed over a bright light and the site of one of the large blood vessels is marked. The egg shell is cut away at this place by a dental disk along an area 1.5 cm. long by 0.2 cm. wide the shell membrane being left intact. The place is moistened with a drop of saliva and a jar covered with mosquito netting and containing one or two mosquitoes infected with *P. gallinaceum* is applied. With a little patience and contrivance the mosquito can be induced to feed. Out of 33 embryos

exposed to mosquitoes in this way 21 died before hatching six were alive but unhatched at the time of writing and 11 hatched out live chicks. In another experiment 24 eggs were bitten by presumably infected mosquitoes and 21 chicks hatched out two chicks showed parasites in the blood within a few days of hatching and died of the infection a few days later. In a third experiment 32 embryos were exposed to presumably infected mosquitoes and 18 chicks hatched out three of these showed infection within a few days.

F. Hocking

STAUBER, L. A. & VAN DYKE H. B. Malarial Infections in the Duck Embryo. *Proc. Soc. Exper. Biol. & Med.* 1945 Feb., v 58, No 2, 125-6.

"Intraembryonic inoculation of duck embryos with the 3T strain of *P. cathemerium* causes reproducible fatal infections with a high level of parasitemia 8-11 days after inoculation. Splenomegaly occurs in these infected embryos. Intraembryonic inoculation of *P. lophurae* produces much more variable results. Infection requires a considerably longer period to develop. This may depend upon the maturity of the erythrocyte in the embryo. Both species of plasmodia can develop in the embryo at either 37°C. or 40°C. Duck embryos can survive the intraembryonic inoculation of ground organs of malaria infected mosquitoes if they are incubated at 40°C.

RIGDON, R. H. A Pathological Study of the Acute Lesions produced by *Plasmodium lophurae* in Young White Pekin Ducks. *Amer. J. Trop. Med.* 1944 Nov. v 24 No. 6 371-7 7 figs.

In this paper the author describes the results of a study of the pathological lesions which occur in young ducks infected with *Plasmodium lophurae* and compares them with the lesions seen in a fatal case of *P. falciparum* infection in a child, and in *P. knowlesi* infection in monkeys. The basic pathological lesions in these three conditions are similar. There is a marked decrease in the number of red blood cells in the spleen of the ducks that either die or are moribund when killed. The pale colour of the viscera is indicative of a severe anaemia. There is pulmonary oedema, and central necrosis in the liver both of which appear to be consequent on an anoxic condition of the myocardium. As a reaction to the anaemia there is extensive hyperplasia of the blood forming tissues which results in the presence of masses of cells in the walls of the larger vessels of all the organs. These masses project into the lumen and may almost occlude the vessels. A series of illustrations depict the appearance of the microscopic pathology of various tissues.

C. M. Wrayson.

SKELER, A. O. & OTT, W. H. Effect of Riboflavin Deficiency on the Course of *Plasmodium lophurae* Infection in Chicks. *J. Infect. Dis.* 1944 Sept.-Oct., v 75 No 2, 175-8 1 fig.

It has recently been reported that biotin deficiency increases the severity of certain avian malarial infections. It seemed of interest, therefore to study the effect of riboflavin deficiency. Accordingly chicks on riboflavin-free diet or on diet deficient in riboflavin were inoculated with *Plasmodium lophurae* and the course of the infection studied. It was found that in contrast to biotin a deficiency of riboflavin decreased the acute infection as judged by the parasite counts. If during the course of the infection riboflavin was administered, the severity of the infection was increased. That this reduced parasite count was not due to restriction of diet was proved by the observation that chicks having an adequate amount of riboflavin while on only half the food of a control group developed an even heavier infection than did the control group.

C. M. Wrayson

THOMPSON P E Changes associated with Acquired Immunity during Initial Infections in Saurian Malaria. *J Infect Dis* 1944 Sept.-Oct v 75 No 2 138-49 7 figs. [16 refs]

A study of the course of *Plasmodium floridense* and *P. mexicanum* infection in lizards has shown that as regards number of parasites number of merozoites per segmenter and presence of crisis forms the same variations occur as are observable in the course of malarial infections in warm blooded animals. After infection there is an increase in the number of parasites in the blood till a definite peak is reached when there supervenes a parasite decline to be followed if death does not ensue by a condition of developed infection. The whole course of these events was however much slower than in warm blooded animals. During the decline pronounced changes occurred in the morphology and staining reactions of the parasites while the mean number of merozoites per segmenter decreased by 19-33 per cent. furthermore there was evidence of increased phagocytosis during the crisis. It was noted that during the subsequent developed infection the changed crisis forms persisted. C M Wenyon

BLACKWATER FEVER.

STEPHENS J W W GORDON R. M. & DAVEY T H. A Case of Blackwater Fever in an African Girl. [Correspondence] *Trans Roy Soc Trop Med & Hyg* 1945 Mar v 38 No. 4 308-10

i. Referring to the statement by SHIRCORE [this *Bulletin* 1945 v 42 185] that he could not recollect the record of any bacteriological examination of the urine and blood in the literature of blackwater fever Stephens mentions three references of the presence of bacteria in the blood and two others of their presence in the urine. The former were STEPHENS and CHRISTOPHERS (*Reports to the Malaria Committee of the Royal Society* 1900 23) CRICHLAW (*Trans R Soc Trop Med Hyg* 1929 v 23 179) and BOINET quoted by CARDAMATIS (*Prog Med* Nos. 37-40). The latter were ROSS (*Lond Sch Hyg Trop Med Mem* 6 1932 196) and GORDON and DAVEY (*Ann Trop Med Parasit* 1935 v 29 439).

ii. Gordon and Davey refer to their paper mentioned above and quote their summary and conclusions in full (see this *Bulletin* 1936 v 33 514 in which the summary and conclusions are also quoted in full) J F Corson

TRYPANOSOMIASIS

FOWLER A F Massive Dose Tryparsamide by Intravenous Drip Method in the Treatment of Trypanosomiasis. *Trans Roy Soc Trop Med & Hyg* 1945 Mar v 38 No 4 297-304 1 fig

At Tamale in the Northern Territories of the Gold Coast the author treated 42 cases of Gambian sleeping sickness with tryparsamide administered by the intravenous drip method. The apparatus was simple consisting of a glass container and rubber tubing the interceptor being improvised by using an intravenous needle and the barrel of a glass urethral syringe. The dose of tryparsamide was about 2 gm. daily for 6-9 days but a day's interval was often necessary after 3 or 4 days owing to exhaustion produced by the high fever which developed during the injections. The dose of tryparsamide was dissolved in two pints of sterile double-distilled water and a hypodermic needle was used to

enter the vein, the patient's arm being immobilized on a splint. A rate of 40 drops a minute allowed the two pints of solution to be given in eight hours.

Trypanosomes were present in the cerebrospinal fluid in 33 of the 42 patients. Eight of the patients were 6-10 years of age, one was between 11-15 years old, and 33 were over 16 years. There were 31 males and 11 females.

In three cases acuity of vision was reduced to the perception of light only. In all the cases, the injection was accompanied by high fever and apparently caused it—the temperature rose rapidly about one hour after the start of the injection and fell rapidly after it ended. It was exhausting to the patients and the author thinks that the seven deaths which occurred were partly due to it, and remarks that it would be interesting to see the effect of using pyrogen-free water for the injection solution.

Results.—The immediate results were very good but sufficient time had not elapsed for judging whether cure had been effected. The 35 patients who survived the treatment lost all their symptoms—in 24 who were periodically examined during 4 to 7 months afterwards the improvement was maintained.

The author does not advise this method for elderly patients but the shortened course of treatment is an advantage when dealing with Africans.

J. F. Corson.

USINGER, R. L. The Triatominae of North and Central America and the West Indies and their Public Health Significance. *Pub Health Bull.* No 288 Wash. 1944 iv+83 12 pls. & 5 figs. [Bibliography.]

This monograph contains a brief account of the relations of triatomine bugs to Chagas's disease, sections on the biology of the bugs, the host relations and geographical distribution. The greater part is occupied by a systematic description of 46 species found in the area under consideration. There are useful tables of vectors and animal reservoirs of *Trypanosoma cruzi*.

Charles Wilcocks.

LEISHMANIASIS.

SEN GUPTA, P. C. Kala-Azar in Bengal—its Incidence and Trends. *Indian Med. Gaz.* 1944 Nov., v 79 No 11 547-52, 2 figs. (1 map)

From the dispensary and hospital statistics for the years 1931-1940 published by the Government of Bengal, and the indications of the trends of incidence on the different districts obtained from the same figures for the years 1924-1942, and the assumption that the population of the districts may be taken as the mean of the populations enumerated in the censuses of 1931 and 1940 the author has calculated the incidence of kala azar in the various districts of Bengal. He finds that the distribution is very unequal. It is low in Bankura and Burdham, while the most affected districts appear to be Murshidabad, Malda and Rajshahi. Jessore, where the first epidemic was reported in 1824 is still one of the bad areas. The figures for the individual districts are given in tables, while the intensities are shown on a kala azar map. It would seem that for the whole of Bengal the mean population is over 54 million and that during a period of ten years 1,146,698 individuals had kala azar. This would give a specific morbidity rate of at least 210 cases per annum for each 100,000 population. The author writes that, in spite of the fact that one of the best specific drugs was synthesized 22 years ago and has been in use since 1923 the incidence of kala azar is so high that it is still one of the grave problems facing the medical and public health authorities of the province.

C. M. Weyon.

JONES Helen RAKE G & HAMRE Dorothy Cultivation of *Leishmania* in the Yolk Sac of the developing Chick Embryo *Amer J Trop Med* 1944 Nov v 24 No 6 381-3

The authors have cultivated strains of *L. donovani*, *L. tropica* and *L. brasiliensis* in the yolk sac of developing chick embryos of 6 to 9 days incubation. The optimal temperature for growth varied from 23° to 28°C. One strain has been carried on for 31 passages. In most cases the growth of leishmania proved lethal to the embryos though there was no invasion of the tissues. The leishmania develop within the yolk cells both as leishmania and leptomonad forms but they also appear to develop in the leptomonad form in the yolk itself. The strain of *L. donovani* which failed to infect hamsters before yolk sac culture was still non infective after 31 passages
C M Wenyon

SEN GUPTA P C Observations on Malaria complicating Kala-Azar *Indian Med Gaz* 1944 Nov v 79 No 11 523-31 4 figs

The paper describes five cases of malaria complicating kala azar. In two a few malarial parasites were found after long search before specific treatment for kala azar had been commenced. The number was too small to account for the fever which was not controlled by quinine though the parasites were banished. In the other three cases persistence of fever at the end of the course of antimony treatment led to the discovery of a malarial infection both parasites and fever disappearing under quinine. It is clear that the antimonials do not influence the malarial parasites and that there appears to be some antagonism between the leishmanial and plasmodial infections
C M Wenyon

ELKERTON L E. Oriental Sore. Atebrin Treatment *Indian Med Gaz* 1944 Nov v 79 No 11 519-21

The cases recorded at the Indian Military Hospital Quetta, for the four years 1936-1939 were 458 109 392 211 (half the year only). It was noteworthy that 63.6 per cent. were in members of a cavalry unit while the majority of others were in transport or other units closely associated with the cavalry lines. This suggests to the author that *Stomoxys calcitrans* may be a vector in addition to the sandfly [BERBERIAN has shown this to be possible see this *Bulletin* 1939 v 38 1034]. The incubation period was on an average six months while the number of sores varied from one to seven. The usual practice at Quetta was to scrape the sore under short general anaesthesia and to dress it weekly with tannic acid powder covered with vaseline gauze. Under these conditions healing occurred in one to ten weeks half the cases being cured within three weeks. The scarring was very slight. Treatment by atebrin injections having been reported by other workers this was given a trial. In cases with secondary bacterial infection the sore is cleaned with hot potassium permanganate compresses (1/5 000). On the following day superficial injections are made radially from several points on the circumference of the sore with a solution of atebrin (0.05 gm. per cc). According to the response injections are repeated every three to five days. The response also determines the daily dressing—weak carbolic ointment an ointment incorporating atebrin or one containing alum to stimulate healing. The time required to bring about a cure was about the same as in the treatment by scraping. However no anaesthetic was required and the resulting scar was minimal. The injection treatment was particularly suitable for lesions on the face.
C M Wenyon

COSTA, O. G. American Leishmaniasis of Frambæal Type. *Arch Dermat & Syph* 1944 Dec., v 50 No. 6 394-5 1 fig

A case is described in which lesions were present on the lower part of each leg. These were soft and papillomatous, and were traversed by grooves which bounded the papillary formation. The lesions were confluent and presented an appearance resembling that of warts, from which diagnosis must be made in these cases. *Leishmania brasiliensis* were found and the Kahn reaction was negative.

Charles Wilcocks.

SKOW, J. S. Unsuccessful Treatment of American Leishmaniasis with Penicillin. Report of a Case. *Arch Dermat & Syph*. 1944 Nov v 50 No. 5 324-5.

A patient in the Panama Zone had developed a granulomatous lesion of the entire nose extending on to the cheeks with lymphangitis and nodular enlargements at the angle of the jaw. *Leishmania* were demonstrated in the lesions. During five days 559 000 units of penicillin were administered intramuscularly and 50 000 units applied locally. There appeared to be some slight improvement in the accompanying cellulitis but there was no indication that healing was taking place, while leishmania were still present in the lesion. After five weeks treatment with tartar emetic (1.6 grammes) the lesion had almost healed.

C. H. Weyon.

FEVERS OF THE TYPHUS GROUP

DARZINS, E. Rickettsienstudien. [Rickettsial Studies.] *Zent f Bakt I. Abt. Orig* 1943 Dec. 11 v 151 No 1 18-20.

The author describes a new method of staining rickettsiae in smears. The reagents used are —(1) A mordant consisting of Lugol's iodine solution and distilled water 25 cc each. The dilution should be made daily and even the undiluted Lugol solution shows signs of falling off after about four weeks.

(2) The stain consists of 0.2 gm. pure thionin, 10 cc. of 98 per cent. alcohol and distilled water to make up to 100 cc. The thionin is dissolved in the alcohol with constant stirring, then the distilled water is gradually added till the dye has been completely dissolved. The solution is filtered through filter paper. The solution is at its best after three days and it can be kept till it shows signs of falling off in its action.

The author has dealt exclusively with films made from yolk-sac cultures so the following remarks apply to these.

The film is kept for 30 seconds in the diluted Lugol solution which is then drained off and, without drying, the film is stained for five seconds in the thionin solution, then washed with distilled water and dried [presumably in air].

Extracellular rickettsiae take on a deep-blue colour and are as sharply defined as small bacteria. They stand out clearly against the polychromatic and transparent background.

Tissues containing large numbers of rickettsiae are brown-reddish in colour otherwise the smear has a brownish granular appearance.

Fully developed cells of the epithelial type are stained lemon yellow. Their nuclei are blue or burgundy-red.

Smears made from 48-hour cultures contain the rickettsiae chiefly in the form of long blue filaments in the cells, but a few grey or black rod-shaped forms also occur. The infected cells are easily recognized by the greyish-black colour of the protoplasm which in uninfected cells is yellow.

In four-day cultures large numbers of extracellular blue-stained rickettsiae are seen in addition to the intracellular forms. The author claims that the method is simple the reagents are easy to obtain and the study of the development of the organisms in cultures is greatly facilitated. *John W D Megaw*

SCHRODER W Ueber die Reifung der agglutinatorischen Kraft des Blutserums in vitro als diagnostisches Kriterium bei Fleckfieber [The Strengthening of Serum Agglutination by Ripening *in vitro* as a Diagnostic Criterion in Typhus Fever] *Zent f Bakt I Abt Orig* 1943 July 20 v 150 No 5 236-43

The author produces evidence to show that the titre of the Weil Felix reaction observed after a combined period of two hours incubation and 22 hours at room temperature is a more reliable indication of typhus infection than the titre observed after two hours incubation. He has found that in cases of typhus the titre may be low after two hours, but after a further 22 hours it usually becomes significantly high whereas in the occasional positive reactions observed in the absence of typhus infection the titre does not rise to the same extent. For example in one table four cases of typhus are shown in which the titre was 1-100 after two hours and in these the readings after 24 hours were $\pm 1-800$ $\pm 1-600$ 1-400 and 1-800 respectively.

In striking contrast the table contains data referring to six cases of other diseases in which the titre after two hours was $\pm 1-200$ in five of these the reading after 24 hours was 1-200 and in the other it was $\pm 1-400$. Also in 12 cases of other diseases in which the reading after two hours was 1-100 the titre never rose above 1-200 after 24 hours. These examples illustrate the general run of the findings though a few cases of typhus are included in the tables in which the later reading was only twice as high as the earlier one and did not reach a significant height. In such cases one or more tests carried out later nearly always gave significant responses.

The conclusion reached was that definitely positive reactions at titres of 1-400 or over were diagnostic of typhus fever except in occasional cases of jaundice in which the titre might rise from 1-100 after two hours to 1-400 after 24 hours.

[In the abstract below WINKLE expresses disapproval of the delayed reading of the reaction] *John W D Megaw*

WINKLE S Untersuchungen zur Weil Felix Reaktion I Mitteilung [Investigations into the Weil-Felix Reaction. Part I.] *Zent. f Bakt. I Abt. Orig* 1943 Dec. 11 v 151 No 1 3-11

The author has investigated the agglutination reactions of large numbers of sera tested with O and H cultures of *Proteus X19* and X2 with HXA (containing also an O element) and with three other strains of *Proteus* organisms.

He defines O-agglutination as being granular in type and H agglutination as flocculent. With O-strains of organisms the reaction is always granular but with H strains which often contain also an O element there may be a combination of the granular (O) and the flocculent (H) types of agglutination.

During 1941 and 1942 sera from 824 patients known or suspected to be suffering from typhus fever were tested of these 310 gave positive reactions with one or more of the *Proteus* A strains at titres of 1-100 or over. The readings were made after two hours incubation at 37°C. the author objects to readings made after a further period of 20 hours at room temperature on the grounds that generally they gave no better results and that they might actually be misleading because the sera of non typhus patients which were completely negative after

two hours sometimes gave positive reactions after 22 hours at titres of 1-100 or even more [see the paper by SCHÄBER, above in which a different opinion is expressed]

Some of the agglutination responses obtained in the 310 positive cases are shown in the Table which is slightly modified for the sake of simplicity

Agglutination responses

No. of Patients	OX19	HV19	OY2	HA2	VK	247	653
184	++	—	—	—	—	—	—
30	++	+	—	+	+(H type)	—	+(H type)
86	++	—	+	—	—	—	—
7	++	+	+	+	+(H type)	—	+(H type)
3	—	+	—	+	++ (O type) and +(H type)	++ (O type)	+(H type)

The *Proteus* organisms 247 and 653 were not of the X type—they were isolated from urine and a stool respectively, in the course of investigations into typhoid fever

It will be seen that 40 of the sera contained H-agglutinins in addition to O-agglutinins, and that all of them gave an H-type of agglutination for *Proteus* 653 which was not agglutinated by any of the 270 sera in which no H-agglutinins were found.

The author discusses the significance of the occurrence of H-agglutinins in typhus sera—he regards this finding as being inconsistent with the various theories put forward to explain the nature of the Weil-Felix reaction—he does not put forward any definite theory but claims that any explanation of this reaction must take into account the not infrequent development of H-agglutinins.

John W D Stegner

WINKLE S Untersuchungen zur Weil-Felix Reaktion. II. Mitteilung [Investigations into the Weil-Felix Reaction. Part II.] *Zent.f. Bakt. I Abt.* Orig. 1943 Dec. 11 v 151 No. 1 11-17

In this paper the author describes a detailed investigation of the agglutination reactions observed in the sera of three Russian patients in whom the reaction was of the VK type [as shown in the last line of the Table in the preceding paper]. These patients gave completely negative reactions with OX19 and OX2—they gave O-reactions with VA at titres rising to 1-800 (11th day) 1-800 (10th day) and 1-400 (11th day)—they also gave H-reactions with VK, HV19 and HA2 at titres ranging from 1-200 to 1-400.

Their reactions with the two *Proteus* strains 247 and 653 not of the V type were —O-agglutination with strain 247 at titres of 1-400 to 1-800 and H-agglutination with strain 653 at titres of 1-100 to 1-200

All the three patients had occupied the same room, and one of them had a slight rash—they had come from the East, and the possibility of mite-borne typhus arose. Although a pure OVK strain was used during part of the investigation described in the preceding paper there was no other case of O-agglutination with VK and in a further series of tests with 6,153 sera from patients suffering from diseases other than typhus this type of reaction was never seen.

There was however a remarkable case of a German soldier from the Eastern Front who had severe septic wounds—he gave completely negative reactions with OX10 and OX2 but a strongly positive O-agglutination with VA and strongly

positive O- and H agglutination with strain 247. There were no grounds for suspecting a rickettsial infection of the mite-borne type so it seemed likely that the patient had been infected by a strain of *Proteus* similar to 247 and that this strain gave rise to the production of the same OAK type of agglutination as occurs in mite borne typhus.

In his conclusions the author expresses the opinion that the non-specific Weil Felix reactions will rarely occur if proper technique is observed.

John W D Megaw

SOPIA F & SPADARO O. Ricerche sperimentali sul virus esantematico. Nota II. Virus storico [Experimental Research into the Virus of Typhus Fever. Note II. Historic Virus.] *Boll Soc Ital di Med e Igiene Trop* (Sera. Eritrea) 1944 v 4 No 2, 353-65. English summary (8 lines)

During an investigation in 1943 infection of the murine type was detected in patients and in rats caught in various parts of Asmara. The present note deals with the investigation of the infection in two out of the five patients seen between November 1943 and January 1944 in these two the infection is regarded as having been of the classical type it was murine in the other three.

From one of the two patients eight successive passages were made through guineapigs the incubation period following the original inoculation was 12-13 days in later passages it ranged from 5 to 10 days. The duration of the fever in the animals was 5-10 days.

Blood from the second patient caused fever lasting two days following an incubation period of 15 days in one of the inoculated guineapigs. One of the guineapigs inoculated from this animal had slight irregular fever and when tested later was found to be fully susceptible to a murine strain of infection from the other guineapig which had a febrile reaction infection was passed through five successive guineapigs.

All but one of the seven passage guineapigs that were tested later proved immune against a murine strain and four others tested against an historic strain were found to be immune.

The authors conclude that the historic type of infection coexists with the murine type in Asmara and they point out that the clinical differentiation of the two forms of the disease is difficult.

[The basic significance of the orchitic and non-orchitic properties of rickettsial strains is regarded by many workers as an incompletely solved problem.]

John W D Megaw

BLANC G & WOODWARD T E. The Infection of *Pediculus albidus* Rudow, the Maggot's Louse on Typhus Carrying Monkeys (*Macacus sylvanus*) *Amer J Trop Med* 1945 Jan. v 25 No 1 33-4 2 figs.

In two experiments the authors found that monkey lice (*Pediculus albidus*) became infected on *Macacus sylvanus* monkeys suffering from epidemic typhus and that the rickettsiae retained their virulence in the lice just as they have been found to do in the case of murine strains after passage through lice and in epidemic strains after passage through fleas.

In one experiment 25 lice collected from a monkey 10 days after recovery from experimentally produced typhus were ground and injected intraperitoneally into a guineapig which reacted typically after an incubation period of three days.

In the other experiment 30 lice were collected from an infected monkey just before death these caused a typical reaction in a guineapig after an incubation

period of five days. Two successive passages of this infection were obtained by inoculation of brain substance through guinea-pigs.

Rickettsiae were found in smears made from pooled suspensions of the intestinal cells of the lice in each experiment.

The authors refer to the experiments of ARKWRIGHT BACOT and DUNCAN [this *Bulletin* 1920 v 15 309] who in 1919 infected a monkey by injecting suspensions made from 150 lice (*Pediculus longiceps*) removed from a typhus-infected monkey (*Macacus rhesus*) just before death. Reference is also made to the experiments of ATKIN and BACOT (*Brit. J. Exper. Path.* 1922, v 3 196) who showed that infected *P. longiceps* could not transmit infection by their bites to a *M. rhesus* monkey—these workers also failed to cause the disease in guinea-pigs by intraperitoneal injection of suspensions of infected monkey louse; they concluded that the typhus rickettsiae probably lost most of their virulence in passage through the unaccustomed host—the monkey louse.

[Although the authors claim that the results of their present experiments and of those previously carried out by BLANC *et al.* [this *Bulletin* 1940 v 37 262 & 573 (*Méd. Tropicales* 1942, v 2, 3)] disprove the provisional view of Atkin and Bacot, they do not appear to have carried out the crucial experiment of transmitting infection by the bites of the insect. The present and other experiments of the kind, show that rickettsiae survive and grow in the intestines of the lice and fleas, but they do not show that the infected insects can transmit infection in natural conditions.]

John W D Megaw

MULLER H. K. Bericht ueber augenärztliche Befunde bei Fleckfieberkranken.
[Report on the Ophthalmological Findings in Typhus Patients.] *Dtsch. Miththeil.* 1943 Mar., v 8 No 3 179-82.

The findings recorded in this report were made in difficult conditions in a War Hospital on the Eastern Front during the months of March April and May 1942. Only one examination could be made of each of the 125 patients who were seen, and the equipment available was of a simple kind.

All the figures in parentheses are percentages.

Externally there was always redness of the conjunctiva, which began to fade after 8-10 days. The other external signs were nystagmus (5) and abnormality of the pupil (9) usually in the form of contraction with a feeble reaction to light or irregularity in the outline.

Changes in the fundus were frequent (92). The most important of these were dilatation of the retinal veins (78) sometimes very pronounced (14) hyperaemia of the optic disk (42) blurring of the edges of the disk (51) elevation of the surface of the disk (19) specific nodular infiltrations in the retina or choroid (28) retinal haemorrhages (14) macular changes (42)—these were, oedema, folding of the surface and loss of the central reflex—contraction of the retinal artery (12) and signs of optic atrophy (5) with or without disturbance of vision.

The typhus nodules were yellow-grey in colour and rounded in outline the smallest were about half the diameter of an artery of the optic disk, the largest were about three times this size, the number varied from 1 to 30 usually 6 to 8. These nodules were regarded as being of great importance in differential diagnosis.

No special relationship could be determined between the severity or incidence of the ocular changes and the gravity of the attack: for instance, among 35 patients who had nodular infiltrations only 16 were suffering from severe attacks—so also oedema of the optic disk and retinal haemorrhages did not seem to be specially frequent in very severe cases.

John W D Megaw

VAINBERG V G & GULAMOVA V P with the collaboration of E P PEREKRIOSTOVA & S G OSTROVSKAYA [Results obtained with the Durand-Krontovskaya Mouse-Lung Typhus Vaccine] *Zhurnal Mikrobiologii Epidemiologii i Immunobiologii* Moscow 1944 Nos 7-8 44-9 [In Russian]

A group of 1871 members of a medical personnel were inoculated with mouse-lung vaccine. Doses of 0.5, 1.0 and 1.0 cc. were given at intervals of seven days. 785 unvaccinated subjects served as controls. During an observation period of eight months 32 cases (1.8 per cent) of typhus occurred in the vaccinated group and 46 (5.9 per cent.) in the controls. Reactions to vaccination were studied in an unstated number of subjects. Local reactions occurred in 601 cases and general in 397 (less than 1 per cent. severe).

Cases in vaccinated subjects occurred at the following times after completion of vaccination: less than 15 days—two; 15 days to 3 months—six; 3 to 6 months—twenty; 6 to 8 months—three. These figures suggest that immunity falls off at 3 to 6 months after vaccination, but this time coincided with the maximum epidemic period (February–April).

The onset of disease was not modified by vaccination so that cases are not likely to be overlooked. The course was generally milder.

Summary of 24 vaccinated and 23 unvaccinated cases

	Vaccinated	Control
Course days	21	23.8
Fever days	11.4	15.3
Type Mild	15	1
Moderate	9	13
Severe	0	9
Fatal	0	4

D J Bauer

RAVIKOVICH E. M. STAROVIEROVA A G NEUMAN A S & MALEVSKY [Epidemiological Studies on the Effects of Anti-Typhus Vaccination.] *Zhurnal Mikrobiologii Epidemiologii i Immunobiologii* Moscow 1944 Nos 7-8 50-54 [In Russian.]

Medical personnel and others particularly exposed to risk of infection (transport workers, launderers, barbers, etc.) were inoculated with mouse lung vaccine. An unvaccinated group served as a control [the numbers in the two groups are not stated]. In assessing the results the records of cases of all types of febrile illness were scrutinized to reveal undiagnosed cases of typhus. Over an observation period of one year the morbidity from typhus in the unvaccinated group was four times as great as that in the vaccinated group.

D J Bauer

RAVIKOVICH E. M. STAROVIEROVA A G NEUMAN A S. MALEVSKY M M & RATNER, S. M. [A Clinical Study of the Effects of Anti-Typhus Vaccination.] *Zhurnal Mikrobiologii Epidemiologii i Immunobiologii* Moscow 1944 Nos. 7-8 54-8 [In Russian.]

An analysis of 57 cases of typhus is given. 12 were in persons who had received anti-typhus vaccination while four were second attacks in unvaccinated subjects. The distribution in age groups was as follows —

Age, years	Vaccinated	Unvaccinated
Up to 29	5	14
30-49	4	13
50 and over	2	4

Mild and moderate forms of the disease predominated in the vaccinated group and severe forms in the unvaccinated —

	Mild	Moderate	Severe	Fatal
Vaccinated	4	4	3	0
Unvaccinated	2	8	21	2
.. second attack	3	1	0	0

The febrile period was of shorter duration in the vaccinated group —

	4-9 days	10-14 days	15 days or longer
Vaccinated	1	9	1
Unvaccinated	3	11	17
.. second attack..	2	2	0

Complications were seen in one vaccinated case (mild bronchitis) and nine unvaccinated (all severe, including seven cases of pneumonia). Most unvaccinated patients had a petechial exanthem, while the vaccinated showed a milder roseolar eruption of shorter duration —

Duration of eruption

	Up to 5 days	6-10 days	11 days or longer
Vaccinated	6	4	1
Unvaccinated	6	13	6
.. second attack	3	1	0

Disease occurred at the following times after vaccination: 11-30 days—three cases (mild); 3 to 6 months—six (five mild or moderate); 9 to 10 months—two (severe). The titre of the Weil-Felix reaction was lower in vaccinated cases and a positive reaction took longer to appear —

Titre ..	Up to 10th day			After 10th day		
	0	≤1/200	1/400	0	≤1/200	1/400
Vaccinated	2	1	3	2	1	4
Unvaccinated	0	2	7	0	4	16
Unvaccinated, second attack				2	0	1

D J Bauer

MONTAÑA J. A. Informe de un brote de tifo ocurrido en Sonsón, Colombia. [Report on an Epidemic of Typhus Fever in Sonsón, Colombia.] *Bolet. Oficina Sanitaria Panamericana* 1944 Oct v 23 No 10 865-75 6 figs & 1 chart English summary

This report deals with an epidemic described as exanthematic typhus but regarded as being of the murine type.

Sonsón is a district of about 1 100 square kilometres in area situated in Colombia between five and six degrees north of the equator at an elevation of 2 500 metres and with an average temperature of 14°C. The population is 35 400 mostly engaged in agriculture. 64 per cent of the people live in rural conditions. Typhus fever is suspected to have existed in the area for many years but it was not till 1942 that cases were diagnosed by laboratory methods.

In the present epidemic the first recognized case occurred in December 1942, and thereafter the number of cases reported in each month from January to July 1943 were 7 21 54 70 72 28 and 7. Among these 257 cases there were 10 deaths all in patients aged 40 years and over. In 119 of the cases the diagnosis was confirmed by Weil-Felix reactions at titres of 1-80 or over in two other cases the titre was 1-40.

Most of the cases occurred in the urban area whose population was about 9 000. About 89 per cent of the houses in this area were infested by *Rattus rattus alexandrinus* but no investigation of the rats or their ectoparasites could be carried out. In the school population (1 612) the infestation rate with head lice was 33 per cent and with body lice 1-68 per cent.

Blood from 10 patients in the febrile stage was inoculated into 20 guinea-pigs. Positive reactions occurred in animals inoculated with the blood of two patients but the responses seem to have been very irregular. One guinea-pig inoculated from one patient had a scrotal reaction, no reference is made to a reaction in the other guinea-pig inoculated from this patient. Blood from the second positive patient caused a febrile response in one guinea-pig whose organs were used for the inoculation of three guinea-pigs, one of these had a scrotal and febrile reaction, another had a febrile reaction and inoculation of its tissues into three more guinea-pigs caused very irregular febrile responses.

The disease was considered to be murine in type because of its mildness (the fatality rate was 3-89 per cent) and the low rate of infestation by lice.

[There is no detailed information regarding the place and time of occurrence of the individual cases. The trend of incidence month by month seems to favour the view that the infection was more likely to have been louse-borne rather than flea-borne but the author states that among the patients (number not stated) personally investigated by him only four were infested by lice and only head lice were found.]

John W. D. Megaw

POLLARD M. & AUGUSTSON G. F. Serological and Entomological Survey of Murine Typhus. *Amer J Trop Med* 1945 Jan., v 25 No. 1 31-2.

The authors claim that their method of detecting the presence of murine-typhus infection among rodents yields positive results in a matter of hours. The investigation was carried out at San Antonio. The technique is as follows.

Trapped rats are placed in insect proof bags and anaesthetized by ether then they are bled to death by withdrawing blood from the heart with a 5 cc. syringe. The blood serum is diluted with an equal quantity of normal saline to avoid heat-coagulation and inactivated at 61°C for half an hour. A complement-fixation test is carried out on serum diluted 1-10 to which 2 units of rickettsial antigen and 2 units of complement are added. The mixture is

incubated at 37°C. for 45 minutes. Amoebocytes and red blood cells are then added, and further incubation is carried out for 30 minutes.

The rat and everted bag are spread out on a white cloth under a strong light, the ectoparasites are picked up and placed in 70 per cent. ethyl alcohol for identification.

In the survey described in the paper 6 out of 34 rats caught in theatres, and 16 out of 30 caught in food establishments gave positive complement-fixation reactions. Ectoparasites were found on all the reacting rats and on some of the negative rats—the total catch on 75 rats (*Rattus alexandrinus*) consisted of 357 tropical rat mites (*Leptonyssus bacoti*) and 44 fleas (*Xenopsylla cheopis*). None of 75 control rats caught in typhus-free localities gave a positive serological reaction and the total catch of ectoparasites consisted of 3 fleas and 4 mites.

In experimentally-infected white rats the complement fixation reaction became positive within one or two weeks, and remained positive up to 120 days at least—no tests were carried out after this period had elapsed.

The finding of infected rats in theatres is regarded as important—it probably explains outbreaks occurring among persons not known to have been exposed to infected surroundings.

John W. D. Megeay

BRIGHAM, G. D. & BINGSTON, I. A. A Study of the Complement Fixation and Weil-Felix Reactions in Wild Rats as related to the Isolation of the Virus of Endemic Typhus. *Pub Health Rep* Wash. 1945 Jan. 12, v 60 No. 2, 29-46. [23 refs.]

By the remarkable investigations described in this report the authors have shown that the complement-fixation reaction is a much more sensitive test of the occurrence of endemic typhus fever among rats than the Weil-Felix reaction which has hitherto been so generally employed.

Sera of 1,392 wild rats from five cities in the U.S.A. yielded 48.7 per cent. of positive complement fixation reactions against 3.6 per cent. of positive Weil-Felix responses.

From Savannah, Ga. 803 rats caught between the end of November 1941 and the end of October 1942 were tested—329 were complement-fixation positive and only three of these, and none of the others, were Weil-Felix positive. Brains of 311 rats from this city were inoculated into guinea-pigs, and from among these 27 strains of endemic typhus rickettsiae were isolated—in 24 of the 27 infective rats the complement-fixation test had been carried out and had been found positive in all but one at titres ranging from 1-32 to 1-8,192.

In a footnote the authors state that all the sera of 129 rats trapped in California, where typhus does not occur were negative with the complement fixation test so they conclude that a positive reaction means typhus infection, past or present.

Among rats caught in the other four cities in which endemic typhus is known to occur the percentages of positive complement fixation reactions in the wild rats were much higher than those of the Weil-Felix reactions.

From the tables it appears that out of a total of 44 wild rats in which the Weil-Felix reaction was positive seven gave negative fixation responses but in six of these the Weil-Felix titre was only 1-20 and in the other it was 1-80.

Among 30 wild rats from which rickettsiae were isolated only five had a positive Weil-Felix reaction, the titres being, 1-80 1-80 1-160 1-320 and 1-320.

Very interesting results were obtained from the investigation of experimentally infected white rats—52 of these were inoculated with a typical strain of endemic typhus and then kept in 13 cages in 12 of which one un inoculated rat was also placed. The inoculated animals were investigated in

groups of four at varying intervals after inoculation with the following results — Out of eight killed on the 6th to the 15th day seven gave positive Weil Felix reactions (1-20 to 1-1,280) but none of the remaining animals killed on the 20th to the 296 days was positive.

All the 45 rats killed from the 6th to the 182nd day gave positive complement fixation reactions at titres ranging from 1-256 to 1-8 192 and six out of seven surviving on the 296th day reacted at titres of 1-128 to 1-512.

Strains of endemic typhus rickettsiae were isolated from the brains of all the rats killed up to the 182nd day but from the remaining seven rats which were not sacrificed attempts to isolate rickettsiae from blood clots failed.

Four of the 12 control rats which had not been inoculated became infected these were the ones killed on the 21st, 29th, 35th and 315th days and all of them had positive complement fixation and negative Weil Felix reactions on the day they were killed.

Full details of the results of the experiments are given in the report but the above general summary is sufficient to show that the authors are justified in stating that the complement fixation test is the most practical means for detecting past or present endemic typhus infection among wild rats. The technique unfortunately is complicated. [See this *Bulletin* 1944 v 41 738.]

John W D Megaw

STEPHENSON R. W. Mite-Borne Typhus in the Anglo-Egyptian Sudan. *Lancet* 1945 Mar 17 341-2.

An attack of fever suspected to be one of the mite borne typhus type occurred in an Englishwoman, aged 39 who had been living in Abu Usher 70 miles south of Khartoum for three weeks before the onset. No cases of clinical typhus had been reported from the area and later Weil Felix tests on a large scale showed a complete absence of positive reactions with *Proteus OX19*, *OXK* and *OX2* in cases of fever occurring in the locality.

The patient had very severe headache for seven days probably also slight fever. On the eighth day a few papules appeared on the abdomen and back the temperature was 99.2°F. Two days later the papules were more numerous they did not extend beyond the trunk the temperature was 101°F on this day and soon it reached 103°F with a daily remission of about one degree. The total duration of the attack was 20 days.

Neither local sore nor gland enlargement could be detected.

The agglutination titres on the 12th day were — *OXK* 1-2 500 *OX19* 1-50 *OX2* negative typhoid H 1-500 typhoid O 1-50 Paratyphoid A and B and melitensis organisms were not agglutinated. The patient had been inoculated with T.A.B. vaccine recently.

Apart from one probable case of tick typhus reported by E. S. HORGAN [Report of the Sudan Medical Service 1941] and a few cases of louse-borne typhus imported from Egypt no other fevers of the typhus group had been reported from the Anglo-Egyptian Sudan. The authors state that the exact type of infection in the present case remains unknown.

[The probable occurrence of mite borne typhus in the neighbouring country Abyssinia has been suggested by ELSDON DEW (this *Bulletin* 1943 v 40 632) who refers to cases of typhus-like fever in which *Proteus OXA* is strongly agglutinated. ROBINSON (*ibid* 686) on the other hand states that in Addis Ababa where mite borne typhus is not known to occur the *OXA* reaction is strongly positive in all cases of relapsing fever. An interesting isolated case of the enigmatic occurrence of *OXA* agglutinins is discussed in an article by WINKLE (above)]

John W D Megaw

Hicks, J. D. Post-Mortem Changes in Scrub Typhus. *Med J Australia* 1945 Jan. 20 v 1 No 3 57-60

This general description of the changes seen after death from scrub typhus is based on 24 autopsies carried out by the author and 11 reported by others. The days of the disease on which 33 of the deaths occurred are shown in the table —

Day of Disease	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
No. of Deaths	1	0	2	1	2	1	4	5	2	3	3	2	2	2	3

The Weil-Felix reaction was positive in all but seven of the 35 cases (presumably with *Proteus OXK*). The skin and subcutaneous tissues in most cases were stained yellow with atabrin (mepacrine) but no suggestion is made that any of the changes described were due to malaria. There is no mention of the existence of differences between the findings in cases in which death occurred early and in those in which it was delayed.

The main changes were proliferation of the reticulo-endothelial tissues and infiltration of the interstitial tissues with large numbers of mononuclear cells (mostly large and small lymphocytes and macrophages but also some plasma cells). This infiltration was most conspicuous in the heart and lungs but it was also pronounced in the spleen, in which vasculitis was more prominent than in the other organs. The capillary endothelium throughout the body was swollen.

Some of the more frequent naked-eye changes were as follows. —The brain was usually soft, and occasionally there was oedema of the leptomeninges or injection of the surface vessels of the cerebrum. Otherwise the brain in most cases looked almost normal.

The pericardial cavity usually contained an excess of fluid in seven cases this amounted to more than 100 cc. The only constant naked-eye change in the heart was pallor and softening of the myocardium.

The lungs showed dark purple firm areas on the surface in some cases, but more often the whole or part of a lobe was in a state of solid congestion. Acute infection, bronchitis or bronchiolitis was present in about one-half of the cases extending to a bronchopneumonia in one-third. An effusion of 50-500 cc. of yellow brown fluid was found in the pleural cavity on one or both sides in about half the cases and in a similar proportion there was free fluid in the peritoneal cavity usually amounting to 100-300 cc.

The liver was enlarged in half the cases occasionally to a very considerable degree. It was usually pale and soft.

The spleen was always enlarged generally to three times the normal size. It was dark-red, soft and friable.

The kidneys showed pale swelling of the cortex and on the inside of this there was a narrow zone of intense congestion.

In one-third of the cases there were 2-3 cc. of clear fluid in the tunica vaginalis sac.

Apart from the microscopical changes already mentioned the following are of interest. —In a few cases the small vessels of the brain were shadowed by round cells, and frequently small haemorrhages were seen, especially in the pons and mid-brain. Congestion of the central veins of the lobules of the liver was usual, and the portal tracts were generally packed with large mononuclear and lymphocyte cells. Most of the normal lymphoid tissue of the spleen was replaced by masses of cell infiltration of the type already referred to. In several

cases pronounced vasculitis occurred in the spleen, this took the form of several layers of round cells beneath the endothelium of the veins

In stained smears made from the tunica vaginalis intracellular particles were found but they could not be diagnosed with certainty as rickettsiae

John W D Megaw

BERRY M. G. JOHNSON A. S. Jr & WARSHAUER, S. E. Tsutsugamushi Fever
Clinical Observation in One Hundred and Ninety-Five Cases. *War Medicine*
Chicago 1945 Feb v 7 No. 2 71-5 1 fig

This study is based on 85 cases observed between December 1942 and June 1944 in two hospitals in New Guinea. There were only two deaths and in both of these cases the chief microscopic lesions seen after death were perivascular cellular infiltration and degenerative changes in the vascular endothelium of the arterioles and capillaries of various organs of the body. Small foci of degeneration of the heart muscle also occurred and in one case a few subpericardial petechial haemorrhages were seen. The authors regard the vascular lesions as of primary importance the myocardial and pulmonary lesions being secondary to them

In addition to the 85 patients admitted directly 110 convalescents were also studied.

In most cases there were prodromata for a few days before the onset which was gradual more often than abrupt with chill. The fever lasted 10-30 days the usual duration was 14-21 days. An eschar with local lymphadenitis occurred in 80 per cent. of the cases any part of the body might be affected but the favourite sites were the scrotum axillae and groins. The spleen was usually palpable

A generalized red maculo-papular rash was seen in almost all the cases. It appeared between the fourth and the eighth day the spots were most abundant on the trunk and limbs the wrists and ankles were rarely affected

Among 60 patients examined by X rays during the second week seven showed evidence of atypical pneumonia and two of empyema. There was a fall in the blood pressure by the end of the first week the systolic reading was usually 90 mm and the diastolic 60 mm. There was no evidence of myocardial failure. Electrocardiograms were made during the fever in nine patients and during convalescence in 21 no abnormality was found in any case

The red-cell counts were usually 4-5 million per cmm. the leucocytes ranged from 4 000 to 8 000 the granulocyte lymphocyte ratio was 6:4

The highest titre of agglutination of *Proteus* OXK was reached about the 20th day the reaction was almost always positive. The Widal test was useless as a means of excluding typhoid fever it was frequently positive in the patients all of whom had been inoculated with T.A.B. vaccine.

Four patients had very severe headache, delirium, and stiffness of the neck. One-third had partial temporary deafness which disappeared in 4-8 weeks

No drug treatment had any effect. Sulphonamides, given to patients who had pneumonia caused no improvement. Absolute rest adequate fluid intake by the mouth, and a generous diet were regarded as important. Intravenous plasma given slowly and in moderate quantity appeared to have some value in certain cases

The authors specially insist that no suggestion of heart disease should ever be made to the patient otherwise an obstinate cardiac neurosis may result. Permanent sequelae are regarded as unlikely to occur

John W D Megaw

LEVINE, H. D. Cardiac Complications of Tsutsugamushi Fever (Scrub Typhus): an Investigation of their Persistence. *War Medicine* Chicago 1945 Feb., v 7 No. 2, 78-81 1 fig. [Refs. in footnotes.]

The author describes mite-borne typhus-like tsutsugamushi fever as being the disease with the highest mortality likely to be encountered by troops in the Australasian Islands. The pathology of the disease is stated to be a widespread perivascular infiltration of lymphocytes and plasma cells. The disease is said to have "none of the tendency of some of the other rickettsioses to produce thromboses or haemorrhages."

[This point of difference cannot be accepted as being of general applicability in the paper by BERRY *et al.* (above) subpericardial haemorrhages are mentioned as occurring in one of the two fatal cases, and haemorrhages in various organs are described in two other recent papers (LIPMAN *et al.* this *Bulletin* 1945 v 42, 371 and HICKS above, p. 554). The fatality rate in the present series is not mentioned if it was as low as in the group dealt with by BERRY *et al.* the infection cannot have been virulent.]

The investigation was undertaken to find whether cardiac changes were likely to persist after attacks of the disease. The records of 130 convalescent patients seen between July 1942 and February 1944 were reviewed, and these were found satisfactory except in 15 cases. The average interval between the onset of the disease and the arrival of the convalescents for cardiological examination was about nine weeks.

During early convalescence 86 of the patients had complained of dyspnoea or palpitation in 37 cases persistent tachycardia, or hypotension, or effort intolerance, was mentioned as having occurred during the period of evacuation through the chain of hospitals on admission to the general hospital, 34 still had symptoms which they or their medical officers, regarded as evidence of cardiac involvement.

Only four of the patients were found to have physical signs of cardiac abnormality and in three of these the signs consisted of systolic murmurs the fourth patient had signs of cardiac enlargement.

Electrocardiographic examination was carried out on 118 patients, and only seven showed major abnormalities of which five proved to be transient. A control observation on 200 persons suffering from gonorrhoea was made and four were found to have abnormalities of the same types, so there was no clear evidence that tsutsugamushi fever was responsible for the electrocardiographic aberrancies.

Among 63 patients investigated by X-ray only five showed any cardiac changes, and none of these was really significant.

The blood pressure was within the normal range (110-140 systolic and 68-90 diastolic) in 126 of the 130 patients in the other four the systolic readings were 90-100 and the diastolic 60-70.

By an analysis on the lines laid down for the diagnosis of functional heart disease by LEWIS and others it was found that at least 49 of the patients were suffering from the syndrome variously described as soldier's heart neuro-circulatory asthenia, effort syndrome etc. this condition is known to be a common sequela of such diseases as typhoid fever pneumonia, influenza, and dengue.

There was evidence that a suggestion had been conveyed to some of the patients during their stay in hospital that tsutsugamushi fever was likely to cause permanent disease of the heart, and that in this way a "practically ineradicable impression" had been implanted in their minds.

Of the 130 patients, only six were evacuated to the U.S.A., and in only two of these the reason was cardiac disease five were discharged to "limited

service two were transferred to a naval hospital the remaining 117 were returned to full military duty

The circulatory disturbances associated with the disease are regarded by the author as being largely due to poor vascular tone associated with the generalized vasculitis which is the chief element in the pathology of tsutsugamushi fever

[These findings are important they agree closely with those of the authors of the preceding paper and they go to show that mite-borne typhus has no greater tendency to cause permanent damage to the heart than other fevers of the typhus group of corresponding severity] *John W D Megaw*

SEN GUPTA P C A Case of Typhus Fever complicating Kala-Azar in Calcutta. *Indian Med Gaz* 1944 Dec. v 79 No 12 602-3

An Indian girl aged four years had almost completed a course of treatment for kala azar and had been free from fever for more than a month when suddenly she was attacked by fever which remained high for 5 or 6 days. Seen at the end of this time she had low fever and a profuse dusky erythematous blotchy rash chiefly on the legs but also on the abdomen and arms not on the face. Neither necrotic ulcer nor marked enlargement of the lymph glands was seen. Recovery was uneventful the rash had disappeared 11 days after it was first seen.

Proteus OXK was agglutinated at a titre of 1-400 on the seventh day of the illness the titre fell to 1-25 on the 10th day and the reaction was negative on the 14th day. Neither *Pr OX19* nor *Pr OX2* was agglutinated.

The type of the agglutination response was regarded as confirming the diagnosis of typhus caused by a strain of rickettsia similar to that of tsutsugamushi fever.

The anomalous nature of the reaction is attributed to the well-recognized fact that patients suffering from or convalescent from kala azar show very poor immunity reactions to other infections.

[No mention is made of the locality in which the patient was living before the onset presumably she was being treated as an out patient at the Kala Azar Clinic.] *John W D Megaw*

YELLOW FEVER.

BRITISH GUIANA. Report on the Yellow Fever (*Anti-Aedes aegypti*) Service of the Medical Department, British Guiana, for the Year 1944 [BEVIER, G M.D. Chief Officer] MS 12 typed pp 3 charts.

The staff of The *Anti-Aedes aegypti* Service consists of one chief officer one medical officer two supervisors two supervising inspectors 17 chief inspectors and some 200 junior employees. The staff during the past year has laboured to diminish the risk of yellow fever in British Guiana especially in Georgetown and as the report shows their efforts have been attended with considerable success for example the breeding of *Aedes* in roof gutters has been greatly reduced. An interesting part of the report is that which deals with the results of examining aeroplanes and trains for the presence of mosquitoes. Altogether 362 aircraft were inspected during the year south bound aircraft came from Trinidad while the majority of those north bound came from Paramaribo but there were a few from Mánados. Two hundred and fifty five of these aircraft were found to be free of insects, the remaining 107 yielded a total of 16 mosquitoes (seven *Culex quinquefasciatus* [C fatigans] eight *Mansonia*

Anopheles and one *Aedes taeniorhynchus*. The examination of trains entering Georgetown from the east coast yielded considerable catches, and BEVIER is of the opinion that trains constitute a constant source of re-infection and that *Anopheles darlingi*, the malaria carrier, was also being brought into Georgetown by this route. During the year 177 catches "were made" the species most frequently found in the trains during the year were *Culex quinquefasciatus* (881 specimens), *Aedes taeniorhynchus* (793) which appeared in April and November and *Anopheles tarsimaculatus* (728) which were most common in May, June and July. There were 412 other *Culex* mosquitoes including 63 *C. nigripalpus*. Only six bromeliad breeders were found, one *Wyeomyia* and five *Microculex*. No cases of clinical yellow fever were discovered during the year.

R. M. Gordon

HARGETT M. V. The Control of Yellow Fever. Puerto Rico J. Pub Health & Trop Med. 1944 Sept. 3-45. 2 maps & 1 chart. [Refs. in footnotes.]

A general summary of some of the literature with special reference to the control of yellow fever.

E. Hinds

PLAGUE.

WAGLE P. M. Sulphadiazine in the Treatment of Bubonic Plague. Indian Med Gaz. 1944 Dec v 79 No. 12, 535-9

This was a well-conducted alternate-case trial of sulphonamides in plague—sulphathiazole which has already been shown effective and sulphadiazine which was a new venture. Altogether 180 cases of genuine plague were treated in strictly alternate succession, 89 with sulphathiazole and 91 with sulphadiazine, with no differentiation of septicæmic and non-septicæmic plague and with mortalities of 33.7 and 21.9 per cent. These favourable mortalities may be compared with a previous trial of iodine intravenously where the mortality for 165 patients was 58.1 per cent. The newer drug sulphadiazine, was administered in initial dose of 4 gm. followed by 2 gm. four hours later and 1 gm. every four hours. The patient received 10 gm. of the drug on the first day and 6 gm. on subsequent days. Still larger doses were given in some very serious cases. All the patients treated with sulphadiazine and some of those treated with sulphathiazole received part (2 gm.) of the initial dose intravenously, all other doses were given by mouth. In no case was the drug given for more than 12 days.

The percentage mortalities mentioned are for all types of plague case, and by excluding those moribund on admission, the mortalities become 12 per cent. for sulphadiazine, 21 per cent. for sulphathiazole and 53 per cent. for iodine. Patients were encouraged to drink plenty of water to secure a urinary output of at least 1,200 to 1,500 cc. daily and no serious toxic reactions occurred.

W. F. Harvey

SAVINO E., KUHN M. J. & MORALES VILLAZON N. Presencia de lesiones de "Resolving Plague" (= peste crónica) en ratas grises. ["Resolving Plague" in Gray Rats.] Rev. Inst. Bacteriol. "Dr. Carlos G. Malbrán" Buenos Aires. 1944 June v 12, No. 2, 190-94. 4 pls. [16 refs.]

Examples of chronic plague are very rare but have a special interest because they furnish evidence of continuance of infection after the cessation of an epizootic and possibly of the means by which infection is carried over through

a non plague season to the next plague season. The present case of chronic plague was the only one that had been met with among 120 000 rats examined between 1938 and 1943. The rat had been caught alive towards the end of a great epizootic and at examination showed little abnormality except for an encapsuled abscess in the spleen filled with caseous material. No plague bacilli were found in the purely splenic tissue but plague bacilli were abundant in the abscess. This then is to be classed as a case of resolving plague in which living plague bacilli still survived.

W F Harvey

BACILLARY DYSENTERY

JACOBY A H LOUDON J R WYNE P S & FAILMEZGER, T R The Diarrhea Problem in a New Guinea Base *Bull U.S Army Med Dept* 1945 Mar No 86 70-78 4 figs

Among 1 400 patients admitted to hospital with diarrhoea bacteriological examination by use of the rectal swab yielded dysentery bacilli in 391 salmonella organisms in 37 and other non lactose fermenters of doubtful pathogenicity in 65 [The culture medium used is not stated] Nearly 80 per cent of the dysentery organisms were Flexner types and only 3.6 per cent were Shiga strains. More than half the diarrhoeal cases were classified as mild infections irrespective of whether a specific pathogen was isolated or not. Different groups of cases were treated with sulphaguanidine alone (3.5 gm four-hourly for one day then 3.5 gm t.i.d.) a course of sulphaguanidine followed by sulphaguanidine 3.5 gm. plus sulphadiazine 1 gm. t.i.d. and sulphaguanidine 3.5 gm plus sulphathiazole 1 gm four hourly for one day and then t.i.d. If stools were still positive after a six-day course a second more intensive course was given. In the dysentery infections the best results were apparently obtained with the sulphaguanidine-sulphathiazole mixture although there was little difference in the average stay in hospital for the three groups. In each of these groups the stay was half or less than that required for a group treated irregularly with miscellaneous sulphonamides. The sulphaguanidine-sulphathiazole mixture was superior to sulphaguanidine alone in the treatment of non-specific diarrhoea. To prevent spread of infection in the hospital each patient was given a card instructing him about personal hygiene sterilization of all mess-gear was insisted upon fly control was practised and food-handlers were kept under medical and bacteriological supervision.

Robert Cruickshank

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

ADAMS A. R. D Amoebiasis with special reference to Treatment. *Trans Roy Soc Trop Med & Hyg* 1945 Mar v 38 No 4 237-44 [26 refs.] Discussion 244-58 [HARGREAVES W H SCOTT H H (President) PRIEST R. MANSON BAHR P LOURIE E. M. HOARE C. A. SMYLY H J WILLMORE J G HODGE E. H V & DREW R ADAMS A. R. D (in reply)]

From his experiences of the treatment of amoebiasis ADAMS until recently believed that the elimination of a gut infection with *E. histolytica* in all but a small proportion of cases was merely a matter of routine. A few preliminary injections of emetine were followed by a three-weeks blunderbuss assault on

the parasites with auremetine stovarsol, bismuth subnitrate by the mouth and retention enemata of chinlofon. He could remember only one case which proved refractory to treatment. In 1943 a batch of 30 cases arrived from the Indian and Burma theatres of war. The patients were bed ridden, emaciated and were passing blood-stained stools containing many amoebae. They proved to be entirely refractory to routine treatment whilst some actually relapsed within a few days. Repetition of the treatment in others eventually proved successful but a residue were still infected, despite any course of treatment. Amongst other methods were the oral administration of sulphaguandine, sulphasuxidine, rectal administration of these compounds in cod liver oil and retention enemata of mepacrine hydrochloride. All produced temporary amelioration, but none showed evidence of specific action on the causative organism.

There appeared to be two explanations of this intractability. Either the men were infected with an unusually virulent and resistant parasite or they had been excessively dosed with emetine long after it was plainly evident that this drug would not sterilize them. As a result the amoebae had become resistant to emetine.

It is possible also that amoebae thus rendered resistant to emetine become at the same time less amenable to any other available drugs. It therefore appears that the whole subject of the treatment of amoebiasis should be approached from a new aspect.

HARGREAVES described his experiences with patients suffering from chronic amoebiasis most of whom had already proved refractory to treatment in other hospitals in England. Some had been under continuous treatment for many months, sometimes as long as two years. He did not criticize the manner in which emetine had been used by medical officers under difficult circumstances, for some patients had actually become acutely ill during the course of 21-day blunderbuss treatment and he had been forced to inject this drug to relieve them. He sincerely believed that it would have been wiser to invade most of these chronic cases earlier. He believed in providing as full a diet as possible and in giving due attention to the psychological aspects of this depressing disease. Until March 1944 he had employed the well-known standard treatment—six daily injections of grain 1 of emetine followed by E.B.I. together with chinlofon retention enemata for 12 days and kathi stovarsol or carbarsone 4 grains twice daily for 12 days. This was compared with Adams's three-weeks course and no advantage was found in the latter (Liverpool) treatment. In a series of 70 cases (54 invalided from India) giving half of them the standard and the other half the Liverpool course—of these 48 were apparently cured and of the remaining 22 (16 of which were from India) 12 improved, but relapsed after a few days and 10 were unchanged.

In addition to the drugs already mentioned (with the exception of diodoquin and mepacrine) he had tried extract of kurchi bark, kurchi bismuth iodide stilbamidine sulphaguandine and sulphasuxidine without success.

Injection of 100 000 units of penicillin intramuscularly followed by 33 000 units three-hourly up to a total of 1 000 000 units was successful in saving the life of one particularly critical case. He put on four stones in weight, but though his physical condition had improved beyond recognition this form of treatment had no effect upon the *E. histolytica*. In the laboratory it had also not been possible to demonstrate that penicillin had any action upon this organism.

On the assumption that secondary bacterial invasion plays a large part in the distressing symptomatology Hargreaves now gives a course of sulphasuxidine, 60 gm. in conjunction with penicillin. This is followed by a standard anti-amoebic course lasting three weeks. When fit for convalescence the patients are discharged for one month prior to re-examination. He felt sure that the

attack on secondary infections rendered the severe refractory cases more amenable to subsequent treatment with specific drugs.

SCOTT drew attention to other drugs notably the seeds of *Brucea javanica*, generally known as *kô-sam*.

PRIEST had had much the same experiences as Hargreaves. A trial of diodoquin was proving encouraging but that was always the case with any new drug in amoebic dysentery. It was also remarkable that even after much emetine or auremetine a patient might suddenly develop amoebic hepatitis.

MANSON BAHK reiterated his conviction that repeated injections of emetine in successive courses in debilitated patients only served to produce an emetine-resistant strain of *E. histolytica*. The physical condition of the patient was all important as amoebic dysentery was the outcome of the resistance of the tissues to invasion by the amoebae. In many of the so-called incurable cases minutiae of treatment had not been observed and emetine-bismuth iodide was often exhibited in keratin-coated capsules which were not absorbed. In several so-called resistant military cases from India he had obtained success by giving this drug in an absorbable form.

LOURIE referred to the experimental production of emetine-resistance in cultures of *E. histolytica*.

HOARE brought forward some evidence that the small race of *E. histolytica* may eventually prove to be non pathogenic to man.

HODGE and DREW concentrated on the criteria of cure in amoebiasis. These are —

- (1) General constitutional recovery
- (2) Absence of thickening or tenderness of the colon and of tenderness or enlargement of the liver
- (3) The absence of vegetative or cystic forms of *E. histolytica* in at least 10 specimens of faeces
- (4) The absence of active ulceration on sigmoidoscopic examination. Some times radiological examination with double contrast barium-air enemata is of value in demonstrating ulceration out of reach of the sigmoidoscope.
- (5) The appendix may constitute the nidus of infection and appendicectomy prove necessary to effect a cure.

P Manson Bahr

LAMB W. L. & ROYSTON G. R. Chronic Amoebiasis. Investigation and Treatment. *Lancet* 1945 Apr 14 455-7 1 chart [11 refs.]

After pointing out the importance of early recognition and thorough treatment of the large numbers of persons with amoebiasis who may be expected to return to Britain from overseas for some years to come the authors classify the drugs which have been employed in the treatment of this condition into four groups. The first group embraces preparations of emetine given either by injection or by mouth the second, organic arsenicals for oral administration the third preparations of the iodo-oxyquinolin-sulphonic acid series given either orally or by rectal injection and the fourth a number of other compounds—bismuth and kurchi by oral, and eusol and silver nitrate by rectal administration.

They discuss briefly the various combinations of these employed by various workers in an endeavour to sterilize chronic relapsing amoebiasis and point out that with any of them there is a good chance of effecting a cure though there is disagreement as to which of them is the best.

In five months of 1944 the authors investigated and treated an unselected group of 81 men all but three of whom had been invalided to the United Kingdom for amoebiasis the majority coming from India and having had previous treatment for a varying number of relapses. All cases with a suggestive history of amoebiasis were sigmoidoscoped, and scrapings were taken from any

ulcers or suspicious-looking areas. The stools were examined microscopically and cultured [on how many occasions and whether for protozoa or for pathogenic bacteria is not stated].

In three cases *Entamoeba histolytica* were found in the stools but not recovered sigmoidoscopically. In four *E. histolytica* were obtained sigmoidoscopically but not on stool examination. Cases with amoebic ulceration [and presumably parasite positive] received a 21-day course of treatment consisting of "Auremetine" and bismuth subnitrate by mouth on the odd days of the course and on the even days "Stovarsol" and bismuth subnitrate by mouth, while retention enemata of "Quinoxyl" were also given, after a preliminary rectal wash-out with sodium bicarbonate solution. All cases during treatment received a full light diet. Three days after the completion of treatment stools were examined after saline purges. If no parasites were found the patients went to a convalescent home for two weeks and then returned for reinvestigation. If all was well they returned to the home for a further two weeks convalescence before going on to a rehabilitation centre at the end of a further three months each case was again reviewed.

The authors state that 29 cases of proved dysentery received the above course. Of these 26 were chronic relapsing cases with histories ranging from five months to five years and having undergone much previous treatment three were fresh, previously untreated cases.

The three previously untreated cases have not been adequately followed up while among the 26 previously treated chronically relapsing cases the authors infer that the relapse rate after treatment was 91 per cent., basing this figure on those cases which were adequately followed up. They state that the relapse rate among these was almost directly proportional to the time of post treatment observation.

[The number of cases adequately followed up from the authors' own account appears to be less than half of the 29 treated. The reviewer has to confess that he cannot follow the figures given and arrive at the same totals as the authors. It is apparent that percentages based on such small numbers may be grossly misleading.]

A. R. D. Adams

SODEMAN W. A. & LEWIS B. O. Amoebic Hepatitis. *Amer J Trop Med*
1945 Jan. v 23 No 1 35-9

The failure of a large number of the current textbooks to delineate this problem clearly or to emphasize its importance has instigated this paper. Absolute diagnosis should be based upon demonstration of the cause of the disease but in hepatic amoebiasis diagnosis and treatment are almost invariably carried out without the demonstration of the presence of *Entamoeba histolytica* in the liver or its discharges.

The records of patients with such diagnosis at the New Orleans Charity Hospital and the Marine Hospital during the past five years have been searched. There were 81 patients, 58 with amoebic hepatic abscess and 23 with amoebic hepatitis. In the 58 with diagnosis of abscess 12 or approximately 20 per cent., presented themselves with symptoms and signs concentrated round the right lower pulmonary area.

Acute and chronic conditions including pleural pain, pneumonia, and, in two pleural effusion, focused attention to the area above the diaphragm. One patient had been treated first for atypical pneumonia, and subsequently for idiopathic pleural effusion for seven months before hepatic changes were found, but the entire group showed, in addition to the pulmonary findings, evidence of hepatic involvement. In the remaining 48 the presenting complaints pointed

to the liver with enlargement tenderness bulging occasional fever chills leucocytosis in 81 per cent. and, in 70 per cent. distinct and sudden onset.

In differential diagnosis bronchogenic carcinoma bronchiectasis basal pneumonia atypical pneumonia, tuberculosis empyema and pleural effusion of possible tuberculous or malignant origin may need consideration. Other probabilities are associated with a purely hepatic picture of cirrhosis malignant disease of the liver acute and chronic cholecystitis peptic ulcer infective hepatitis pyogenic liver abscess and hydatid cyst. But this formidable list does not represent all the conditions with which hepatic amoebiasis may be confused. In temperate countries some of these conditions are admittedly many times more common than hepatic amoebiasis but this is hardly true in tropical areas where it is of much more frequent occurrence though this possibility does not always spring to mind. Awareness of the probable occurrence of hepatic amoebiasis was the most important single factor in directing the early establishment of the diagnosis. Without it the diagnoses were either late or accidental. The data and their frequency in 58 patients diagnosed as abscess were —

- | | |
|---|---------------------|
| 1 A history of diarrhoea or dysentery or its presence with hepatic picture | 19 (32.7 per cent.) |
| 2 The presence of <i>E. histolytica</i> in the faeces | 10 (29.4 per cent.) |
| 3 X-ray appearance of fixed right diaphragm, bulging of the diaphragm especially centrally and anteriorly bulging of the right diaphragm with pleural or pulmonary involvement or evidence of hepatic enlargement | 47 (81 per cent.) |
| 4 Chocolate sauce pus (a) from rupture or (b) by aspiration from the pleura or liver | 55 (94.8 per cent.) |

Colonic infection probably always precedes the hepatic lesion but is usually not clinically active. In only 32 per cent. was a history of diarrhoea obtainable. In 11 per cent. the onset was with diarrhoea.

In only 11 (19 per cent.) were X-ray positive findings absent. In 15 (26 per cent.) characteristic diaphragmatic bulging was seen. In 18 (31 per cent.) elevation and impaired movement of the diaphragm and in 14 (24 per cent.) there were similar evidences in association with changes in the pleura and right lower lobe of the lung. These findings constitute important guides for aspiration of pus. In 11 per cent. rupture occurred into a bronchus producing typical sputum. In 15 (26 per cent.) X-ray appearances were insufficient to warrant tentative diagnosis. Of 18 with elevation of the diaphragm, in 11 pus was obtained by aspiration and in five at operation. Further development of and more widespread use of the complement fixation test is sorely needed in hepatic disease.

The history and physical examination centred around a hepatic clinical picture are not by themselves sufficient to warrant the increasing use of emetine as a therapeutic test until other diagnoses are improbable and awareness of the possibility of amoebic infection has led to tests for colonic amoebiasis—X-ray examination of the liver area a complement fixation test or exploration for pus. In this group 78 patients were treated with 6 to 12 grains of emetine hydrochloride. Only once did untoward symptoms ensue and these were cardiac.

P. Manson Bahr

ANDERSON H. H. & CHUAN T. T. H. Comparative Amebicidal Activity of Phenyl Araine Oxide (Mapharsen) related Arsenicals and other Agents. *Amer. J. Trop. Med.* 1944 Nov. v. 24 No. 6 367-9 [14 refs.]

Of the group of agents tested *in vitro* on cultures of *E. histolytica* mapharsen was most effective in that it killed the amoebae in 48 hours when in dilutions of

1 in 20 000 to 1 in 30 000. Of the other substances tested 2,4-dihydroxyphenylarsonic acid was effective in 1 in 8 000 dilution and N,N-disodium formaldehyde bisulphite-3,3-diamino-4,4-di(β-hydroxyethoxy)arsenobenzene in a dilution of 1 in 3 000. Other allied substances had no appreciable effect. The amoebicidal activity of emetine was tested as a control. To be effective concentrations greater than 1 in 25,000 reported by DOBELL and LAIDLAW [this *Bulletin* 1927 v 24 363] were required. The culture technique in the coagulated egg medium of these two observers was employed. In a table the various results obtained are set forth. C. M. Wenyon

RELAPSING FEVER AND OTHER SPIROCHAETOSSES

COSHEM A. G. Relapsing Fever in Panama. Report of Six Cases. *War Medicine* Chicago. 1945 Jan v 7 No. 1 19-22, 2 charts [12 refs.]

In the spring of 1942, during a period of eight weeks, six patients with relapsing fever were seen at the Panama hospital where the author was serving. All showed the usual clinical symptoms and the benignity of the course of the disease was consistent with previous observations. The only two cases showing a relapse are described in detail.

The presumptive exposure of three of the patients to infection on only one night suggested an incubation period of 12 to 14 days. The disease is almost certainly the tick borne type of relapsing fever endemic in Central America.

The intravenous injection of 0.4 to 0.5 gm. of neosarphenamine given soon after the diagnosis was established, followed by a second injection after 3 to 5 days caused the disappearance of all spirochaetes within 24 hours after the first injection and there were no relapses after treatment. E. HANDLE

PAVLOVSKIY E. N. *Dymyomys nitidulus* Pall. as a possible Reservoir of the Virus of Tick Relapsing Fever. *C. R. Acad. Sci. URSS* Moscow 1943 v 30 No. 7 226-8. [Summary taken from *Rev. Applied Entom.* Ser. B 1945 Feb., v 33 Pt. 2 14-15.]

Details are given of experiments showing that *Dymyomys nitidulus*, a small rodent widely distributed in Central Asia and European Russia, is very readily infected with the spirochaetes of tick-borne relapsing fever. The infections were produced by inoculation of the blood of guinea-pigs harbouring a Tadzhikistan strain transmitted by *Ornithodoros tholozani* Lab. & Ménéz (*papillipes* Bl.) or a Georgian strain transmitted by *O. verrucosus* Olen. Zasl. & Fen. or by the feeding of examples of *O. tholozani* infected with another Tadzhikistan strain. Most of the animals survived the infection and the spirochaetes persisted in their blood for up to 32 days.

In nature *D. nitidulus* is associated with woods and the species of *Ornithodoros* are not, but it might serve as host for *O. tholozani* or *O. tartakowskyi* Olen. in Central Asia in cases or along the edges of woodland in the mountains and thus act as a reservoir of relapsing fever.

PAVLOVSKIY E. N. [A Register of the Spirochaetes of Tick Strains of Relapsing Fever in the USSR and Neighbouring Countries.] *Probl. region. Parazit.* Moscow 1939 v 3 19-35 9 figs. [12 refs.] [In Russian. English summary pp. 30-44.] [Summary taken from *Rev. Applied Entom.* Ser. B 1945 Feb. v 33 Pt. 2, 17-18.]

Laboratories in the Russian Union have maintained a number of strains of spirochaetes of tick-borne relapsing fever for years by keeping them in live

examples of *Ornithodoros tholozani* Lab & Megn. (*papillipes* Bir) a method that avoids the expense of repeated passages through guineapigs. The ticks are long lived and have been shown to preserve virulent spirochaetes for 7-8 years and any strains required for experiment can be obtained by feeding the ticks on guineapigs.

Since the rich collection of spirochaetes already made is continuously being increased by the finding of further batches of spontaneously infected ticks the author has begun the publication of a series of records of the strains isolated from ticks in the Russian Union and adjacent countries in places where relapsing fever is prevalent. This paper is the first of the series and also contains details of the records desired. Each should include the identity of the tick, a general geographical description of the place where it was found with a map details of the biotope with illustrations the dates of collection and demonstrations of infectivity of the tick the species of animal used to demonstrate its infectivity the pathogenicity of the strain to man and the names of those responsible for each phase of the work. In this first series particulars are given relating to ten strains of relapsing fever spirochaetes isolated from *O. tholozani* in Tadzhikistan and southern Kirghizia.

PAVLOVSKIĖ E. N. & ALUMOV A. I. [Tick-borne Relapsing Fever in Southern Kirghizia.] *Probl. region. Parazit. Moscow* 1939 v. 3 72-88 4 figs. [In Russian. English summary.] [Summary taken from *Rev. Applied Entom.* Ser. B. 1945 Feb. v. 33 Pt. 2 18.]

During investigations on tick borne relapsing fever in the south western part of the Kirgiz Republic in July and August 1935 many engorged and unfed nymphs and adults of *Ornithodoros tholozani* Lab & Megn. (*papillipes* Bir) were found in several neighbouring districts in artificial caves in which grain was stored or sheep were kept in winter in burrows of rodents and tortoises and in holes inhabited by birds and engorged females had previously been taken in a house. Ticks from a porcupine burrow and burrows of *Meriones erythronus* transmitted spirochaetes to guineapigs on which they were fed. No natural infection was found in small rodents taken in one of the districts but an example of *M. erythronus* was experimentally infected with a strain of spirochaetes isolated from ticks which suggests that this gerbille may be a local reservoir.

Most of the local cases of relapsing fever were evidently tick-borne since the blood of the patients was infective to guineapigs. The disease occurred almost exclusively in spring and summer and a man was experimentally infected with it by the feeding of a batch of *O. tholozani* taken in one of the caves.

Experiments with several strains of relapsing fever spirochaetes from various parts of Central Asia showed that they could not be differentiated by the character of the disease they produced in guineapigs or with any reliability by cross-immunity tests.

SHELDON W. H. Lesions of Muscle in Spirochetal Jaundice (Weil's Disease Spirochetosis Icterohemorrhagica) *Arch. Intern. Med.* 1945 Feb. v. 75 No. 2 119-24 4 figs.

A description of the lesions encountered in 16 biopsy specimens from muscles of the calf of seven patients with Weil's disease seen recently at Grady Hospital Atlanta Georgia.

One of the patients was a white man the others were negroes. All had a history of exposure to rats. Varying degrees of jaundice and enlargement of the liver were observed in every instance. The general clinical symptoms were typical one case was fatal on the third day.

The biopsy specimens were taken at various stages ranging from the 10th to the 68th day of the disease. Early but definite lesions were present in the muscle on the 10th day and clinical relapses were marked by the appearance of new lesions in addition to the existing older ones. The morphological characteristics of these lesions are considered to be rather typical of the disease. The lesions always involved only a part of one muscle fibre and sometimes two or three adjoining fibres showed focal involvement. The earliest change consisted in the appearance of small and medium-sized vacuoles in the cytoplasm of the striated muscle fibre. This tended to become confluent and simultaneously the cytoplasm of the fibre in the involved area lost its cellular detail. The fibrils disappeared but at this stage there was no significant cellular reaction or haemorrhage thus distinguishing it from Zenker's degeneration. The lesions were repaired from about the 17th day onwards by regeneration of the striated muscle without significant participation of the adjacent interstitial connective tissue. At this stage no appreciable fibrosis or scarring occurs but in more severe lesions repair is accompanied by fibrosis. The author examined control sections of gastrocnemius muscle from patients suffering from various other diseases but no lesions resembling those of Weil's disease were observed. It is suggested therefore that biopsy of the calf muscle may be a useful measure in the diagnosis of Weil's disease.

In an appendix, details are given of the examination of biopsy specimens from 12 other patients with suspected Weil's disease. In five cases lesions of Weil's disease were found although in only one of these patients was there a positive agglutination test. One case was doubtful and the other six typhus (1) infectious hepatitis (3) reaction to arphenamine therapy (1) and atypical pneumonia (1) gave negative results.

E. Hindle

LEPROSY

IGNACIO CHALA H., J. & LIERAS RESTREPO F. Estudio experimental sobre algunos bacilos ácido-resistentes obtenidos de material leproso humano (Nota preliminar) [Experimental Study of Acid-fast Bacteria Isolated from Cases of Human Leprosy] Publicaciones del Instituto Federico Lleras Acosta Bogotá 1944 Nov. 31 pp 10 figs (4 pages of refs.)

Six strains of acid fast bacteria isolated from leprosy lesions in man have been cultivated and these form the subject of this work. The authors have investigated their pathogenicity and the results of inoculation experiments in laboratory animals. 381 white mice, 66 guinea-pigs, 68 rabbits, 11 *Alacaras* (*Alacaras mulattii*), 41 fowls and pigeons. The article is so crowded with information that abstract is hardly possible those interested must consult the original. The English summary is so full and so accurate compared with the text, that there will be little or no difficulty in doing this.

The sources of the six strains, the method of cultivation and characters of the growths are detailed. Doses of the bacilli suspended in saline, varying between 0.01 and 3.0 cc. were inoculated by various routes: intradermal, subcutaneous, peritoneal, by mouth, and by nasal insufflation. The macroscopical and histological findings are described. Serological reactions (fixation of complement) were tested before the animals received their injections and again subsequently. In the case of the latter the Lleras-Acosta strain gave a positive in 30.7 per cent. a culture of an organism obtained from the sternal marrow 19.2 Duval's organism 7.6 Kedrowsky's 2.3 one sent from the National Institute of Health Washington 12.3 and one from a human leproma 36.1 per cent.

Besides inoculating the healthy animals with the various bacteria the authors in some cases made the inoculations after performing splenectomy to see if sensitization or greater susceptibility to infection resulted therefrom but with negative results. Animals still alive are being reinoculated and kept under observation and any definite findings are to be reported later. Photographs of animals presenting the grosser lesions are reproduced together with photomicrographs of the histological changes
H Harold Scott

CERRUTI H. Considerações histopatológicas sobre a lepra da mucosa nasal. [Histopathology of the Nasal Mucosa in Leprosy] *Rev Brasileira Leprologia* S Paulo 1944 Dec v, 12 No 4 309-64 18 figs. [Bibliography] English summary

The author has examined sections of tissue from the nasal septa some taken by biopsy 46 from the same number of patients from whom a specimen was taken from one side only and 120 from 60 patients specimens being taken from both sides—168 specimens from living subjects. Another 24 were taken post mortem. The tissues were fixed in 10 per cent formalin and then embedded in paraffin or sections were prepared by the freezing method. Sections were cut at different levels and stained in several ways haematoxylin and eosin the orcein hydrochloride method for elastic fibres and the Faraco technique for staining Hansen's bacilli. Frozen sections were stained by haematoxylin and Scharlach R. The author then describes in great detail the changes but these are set forth more demonstrably in the excellent series of photo-micrographs than can be followed in the minutely descriptive text. He divides the lesions into two main groups those correlated with the leprotic process (such as might occur with other chronic inflammatory conditions) keratosis erosions oedema, congestion and small haemorrhagic foci sclerosis hyalinization and so forth secondly those peculiar to leprosy such as periglandular lepromatous infiltration perivascular (including perilymphatic) infiltration, the macrophage lepra cells of Virchow bacillary invasion of the nerve filaments with thickening of the sheath and degeneration of the fibrils.

He describes these as they appear in the follicular or sarcoid types of tuberculous leprosy. In his comments he notes that some of these changes may be seen in patients who clinically appear to be normal and, therefore, such examinations may be useful and important in early diagnosis of the disease and especially in contacts. [The photographs of the sections showing the tissue changes are excellently reproduced and the article is documented by a bibliography of over 400 references]
H Harold Scott

DE SOUZA A. R. Síndrome de Claude Bernard Horner na lepra. [The Claude Bernard-Horner Syndrome in Leprosy] *Rev Brasileira Leprologia* S Paulo 1944 Dec v 12 No 3 379-82

Three signs characterize the Claude Bernard Horner syndrome ptosis (or pseudoptosis) enophthalmia and myosis to these may be added varied pigmentation of the iris (heterochromia) and lowered ocular tension. Under these conditions pinching of the skin of the neck fails to cause dilatation of the pupil, the eye symptoms are not affected by instillation of cocaine but local application of atropine by lowering the tone of the iris results in disappearance of the myosis. The syndrome is due to sympathetic affection but may be found in those of the medulla, the nerve roots or the ganglia.

The patient in whom this was observed and whose case is here recorded was a Spaniard aged 56 years from S Paulo. The first sign of leprosy which he noticed was an anaesthesia of the left thumb when he was 40 years old. Now the signs are well developed—infiltration of the ears cheeks, nose and supraciliary

ridges, maculae on arms and trunk, etc. Leprosy bacilli were found in the nasal mucus and the skin lesions: blood Wassermann and Kahn were 3-plus, spinal fluid negative.

In the discussion the author enumerates the causes of the syndrome or the conditions in which it occurs such as wounds of the sympathetic, compression by enlarged thyroid or lymphatic glands, lymphosarcoma, granuloma, abscess, vertebral lesions, aneurysm, carcinoma of oesophagus, pleural adhesions, syringomyelia, tabes. He states that in this case none of these was discoverable and "syphilis, tuberculosis and tumours were looked for without result [but his serum gave a 3-plus to the Wassermann and Kahn tests] and he wonders whether leprosy itself may cause it. He has examined 800 lepers in the Santo Angelo leper colony but found no other like the one he records.

H Harold Scott.

GUELLES CASALS, D. *Lepra e hiperestesia ungueal* [Leprosy and Onychalgia.] *Rev Sifilografia, Leprologia y Dermatologia*. Marianao, Cuba. 1945 Jan., v 2, No. 1 55-6.

Onychalgia, or ungual hyperaesthesia of Oppenheim, is a rare condition reported apparently first by Oppenheim in 1903 and seen for the first time in Cuba by Argüelles Casals in 1942 (*Rev Med Cubana* 1942, v 53 1041). The nails *appear* to be quite normal but are exquisitely tender. (From the description, it would seem that the tips of the thumbs and fingers rather than the nail areas are the sites of pain.) Buttoning up the clothes, tying a shoe-lace, playing the piano, typing, wearing gloves for example, are impossible. Cutting the nails is associated with most acute pain which persists after the operation. Oppenheim considers it to be a "neurosis" [which does not explain much] and says it runs in members of "neurotic families"—the treatment recommended is bromism and psychotherapy.

The author records a case in a woman of 66 years who had suffered from the stromatous form of leprosy for four years and for the last two months with a onychalgia in both hands. Buttoning the clothes, cutting the nails or even light pressure on them is acutely painful and brings tears to her eyes. Though her toes were not affected when the author saw her she said that she had had the in there earlier and that it had disappeared in the course of her treatment with antimoogra oil.

The author does not consider the question whether leprosy can produce this condition, but states definitely that they are quite distinct since Oppenheim's syndrome is not associated with peripheral neuritis whereas the pain in leprosy is pleasurable by the neuritis. [This is of course a mere begging the question and does not rule out the possibility of leprosy being one cause of the syndrome.]

H Harold Scott

NEBERG, A. *Valor prognostico da lepromina-reacção de Mitsuda*. Observação de 455 casos durante 5-6 anos [Prognostic Value of Mitsuda's Lepromin Reaction.] *Rev Brasileira Leprologia*. S. Paulo. 1944 Dec., v 12, No. 4 367-77. 2 charts. English summary.

From among a large number of persons on whom the lepromin reaction had been carried out during 1938-37 the author has followed up 445 who were in good health physically, were bacteriologically negative and were undergoing outpatient treatment at dispensaries. This follow-up has continued for 5-6 years to 1942. This total 323 have shown no clinical change and have remained bacteriologically negative. 86 have developed symptoms of the lepromatous type of evolution—skin maculae, infiltrations, bacteria present. Twenty-seven have undergone pericardial development—annular lesions, sarcomas, but bacteriologically negative.

nine are not characteristic they present fresh maculae and are bacterially negative and cannot be placed in either of the other two groups [see this *Bulletin* 1934 v 31 12] The accompanying Table gives the results of the lepromin reactions in these cases —

Lepromin reaction	Reactivation			Unchanged	Total
	Lepromatous	Not characteristic	Tuberculoid		
—	54	6	2	29	91
+	32	3	5	61	101
++	0	0	13	93	106
+++	0	0	7	140	147
Totals	86	9	27	323	445

From this it will be seen that among 91 lepromin-negative cases there were, in percentages 59.3 lepromatous 6.6 non-characteristic 2.2 tuberculoid 31.8 were unchanged among the 101 giving the one plus reaction the percentages are practically those written as totals of the 2-plus 12.2 per cent. were tuberculoid while 87.8 were unchanged and of the 3-plus 4.7 per cent. were of the tuberculoid type

In a similar way the author has investigated 182 non-characteristic cases and Table II gives the results of these —

Lepromin reaction	Reactivation			Unchanged	Total
	Lepromatous	Not characteristic	Tuberculoid		
—	10	5	2	4	21
+	11	1	2	30	44
++	0	0	7	52	59
+++	0	0	1	57	58
Totals	21	6	12	143	182

Detailed observations on these are not necessary but it will be seen how marked is the tendency for negative or one-plus reactions to relapse with the lepromatous forms. The author concludes. These results confirm the possibility of the prognostic utilization of the LT [lepromin test] which would permit the prophylactic services to concentrate on the follow-up of the negative and weak positive reactors prone to frequent relapses of the contagious type.

H. Harold Scott

HELMINTHIASIS

VASILKOVA, Z. G. [The Problem of the Purification of the Water of the River Moskva from the Eggs of Helminths.] *Med. Parasit. & Parasitic. Dis.* Moscow 1944 v 13 No 5 11-16 2 figs. [In Russian]

The author investigated a part of the River Moskva 34 kilometres long which passes through a thickly populated industrial region. Samples were taken from

both banks and at different depths and also during all seasons of 1940 and 1941 from the various waterways of a sewage works whose main outlet discharges into the river. This outlet was the main source of contamination of the river water with helminth eggs but they also came from household drains, industrial sewage and natural waterways entering the river. The samples were filtered and the filtrate was examined for eggs either wet or after drying and clearing of the eggs with clove or cedarwood oil. The viability of the eggs was tested in a moist chamber at 20-24 C.

In the water from the sewage works, 4,500 helminth eggs per cu. m. were found. The eggs were those of *Ascaris*, *Trichuris*, *Taenia* and *Diphyllobothrium* ("Broad ribbon"). In the Moskva River water there were in addition to the eggs of these species those of *Euterobius* and *Microcoelium*. In this river water the following percentages of eggs were found: *Ascaris* 86.6, *Trichuris* 4, *Euterobius* 0.4, *Taenia* 3, *Diphyllobothrium* 5.5, *Microcoelium* 0.4. [It is unfortunate that Russian helminthologists so often omit the generic and specific names. Much confusion would be avoided if the Latin names were given.]

Sampling at different depths on both banks of the River Moskva showed that some natural purification occurs by the settling of the eggs to the bottom of the river. The degree of this natural cleansing depends upon the speed of the current and the depth and volume of the water. The author calculates that there is a natural cleansing in this way to the degree of 69 per cent. in 32 km. during 103 hours. Thus at a village 2.5 km. above the entry of the main outlet of the sewage works, there were 29 eggs (of all species) per cu. m. at a village 2.5 km. below this outlet, there were 263 eggs per cu. m. 32 km. lower down below an intervening dam, there were 91 eggs per cu. m. The eggs were most numerous in samples taken on the left bank, on which the sewage works are situated, but on the right bank the highest number was found at the dam, possibly because of incomplete mixture of the water. Of 49 samples taken 2.5 km. above the entry of the sewage works outlet, 15 (30 per cent.) contained eggs. Of 154 samples taken below this outlet 71 (46.4 per cent.) contained them. The author treats his results statistically. Study of the eggs showed that 67.6 per cent. of the *Ascaris* eggs became embryonated in the normal time under laboratory conditions while 11 per cent. were infertile and 23 per cent. were not viable. In the eggs of *Taenia* and *Euterobius* no externally visible change was seen, but the eggs of *Trichuris* and *Diphyllobothrium* were often deformed. The author thinks it is possible that the people may infect themselves from the river water by drinking it unboiled, by watering kitchen gardens with it and then eating uncooked vegetables, or by bathing. Better methods of purifying sewage water (such as the use of slag or sand filters after sedimentation, properly functioning filter beds and tanks without overloading) and helminthological examination of it are suggested.

G. Lepage

WASHINGTON. A Symposium on Anthelmintics. 334 pp. [Bibliography.] 1942.
Published by the Proprietary Association of America, 810 Eighteenth Street, N.W., Washington, D.C.

This volume is a collection of extracts from the very extensive literature on anthelmintics and comprises selections from hundreds of papers. The helminthics dealt with are *Aspidium*, Carbon tetrachloride, *Chenopodium*, *Beternine*, *Pepo*, *Santonin*, *Spigelia*, Tetrachlorethylene and Thymol.

"The excerpts contained in these monographs reflect the medical and scientific opinion, experience and evidence of a substantial number of authorities. That there exist marked differences of opinion will be apparent. The single purpose of this undertaking has been to assemble recorded data without consideration of the nature of the opinions or the results of experiments."

It is evident that so great a collection of information and opinion placed so easily and relatively compactly at the disposal of the reader will be an invaluable aid to those studying the subject and to those who may have to make plans for the treatment of helminthic diseases on a large scale in the countries where these affections are prevalent

Charles Wilcocks

PARANJAPÉ K D PHALNIKAR N L BHIDE B V & NARGUND K S *In vitro* Observations on the Anthelmintic Action of some Synthetic Lactones and Compounds allied to Santonin. *J Indian Med Ass* 1945 Jan v 14 No 4 69-73 [17 refs.]

The authors set out to discover which of a series of lactones and compounds related to santonin which have been synthesized by NARGUND *et al* (*Rasayanam* 1943 v 8 233 and *J Univ Bombay* 1940 v 9 145) are capable of being good anthelmintics. Some of the earlier literature is discussed. The authors refer to earlier workers who studied the *in vitro* action of drugs upon roundworms. They however found it difficult to obtain roundworms and difficult to keep them alive and therefore decided to test their compounds upon three local species of the earthworm *Pheretima elongata* and upon small freshwater fish [the species is not stated but young specimens 4 to 5 cm. long were used]. The authors discuss the validity of tests done on these animals. They record that CHOPRA and CHANDLER (*Anthelmintics and their use in medical and veterinary practice* 1928) point out that earthworms and helminths belong to totally different zoological groups so that experiments done on the former can only be rough guides at best. The authors accept however the recommendations of the International Conference at Edinburgh and Geneva (no ref.) and of the Hygiene Committee of the League of Nations of the method of SOLLMANN (*J Pharm & Exper Therap* 1918 v 12 129) who regards the authors say the action of anthelmintics upon earthworms as similar to their action upon helminths. The authors therefore used Sollmann's simple immersion method. Three earthworms of about the same size and also the fish were immersed in 100 cc. of solutions of the substances tested. The concentrations of these substances were 0.02, 0.015, 0.01 and 0.005 [per cent. presumably]. Controls were done with a 0.02 per cent. solution of santonin.

For the results the paper must be consulted. The structural chemical formulae of the compounds tested are given. The authors conclude that the simple dienones are likely to prove to be good anthelmintics and that some of the lactones tested are worth further trial.

[If further trial is made the method of BALDWIN (this *Bulletin* 1944 v 41 54) might be tried. This method uses *Ascaris lumbricoides* of the pig and gives kymographic records of the effects of the drugs. Baldwin also discusses the validity of experiments done upon earthworms referring to the strong criticism made by LAMSON and WARD (*Science* 1936 Sept 25 293) of the use of annelids. These authors found no correlation of the action of 121 chemical compounds on earthworms and pig *Ascaris*. Baldwin has no doubt that the neuromuscular mechanism of *Ascaris* differs fundamentally from that of earthworms. Since he found that santonin acts mainly upon the nerve ring in the anterior region of *Ascaris* and that the lactones pilocarpine, strophanthine and umbelliferone had no effect upon *Ascaris* this point would seem to be important. The method of LAMSON and BROWN (this *Bulletin* 1936 v 33 577) which observes the effects of solutions of anthelmintic substances upon *Ascaris lumbricoides* immersed in them is an additional alternative to the use for experiments of this kind of animals which are not helminths.]

G. Lapage

CASTRO G J Hidatidosis ósea. [Hydatid Disease of Bone.] *Rev Med. de Chile* 1944 Dec. v 72 No 12 1074-7, 1 fig

The author records two cases of hydatid disease of the tibia in his own practice and adds comments on the condition based largely on a monograph on the subject by Professor Oscar IVANISEVICH of Buenos Aires. The histories are in many respects similar in the two cases. diagnosis is usually delayed and at first erroneous. hence it may be well to present them fairly fully.

The first patient was a man of 25 years who 15 years before had been operated upon for hydatid of the liver. This seems to have been entirely overlooked when he was admitted in 1935 with a fracture of the right leg at the junction of the upper and middle thirds of the tibia. It was put up in plaster of Paris but after 60 days there was no union and the plaster was re-applied for 80 days. Still there was no consolidation but a pseudarthrosis. In view of a doubtfully positive Kahn reaction he was given antisyphilitic treatment without benefit. Radiograms then showed several clear areas in the bone varying in size without periosteal reaction or local sclerosis. Operation was performed and several hydatids removed. The tibia was reduced to a mere shell. He left hospital with a plaster splint and did not return. all that is known of his subsequent history is that he died of pneumonia about a year later.

The second patient was a professor 48 years of age who came to the hospital in June 1944. Four years before when walking he fell and broke his left leg at the junction of the upper and middle thirds of the tibia. A plaster splint was applied. This was removed after 45 days and he was told to rest the limb and have it massaged. He suffered more or less continuously afterwards from pain and could only get along with crutches. He again went to hospital. mal-union was diagnosed and operation was undertaken to rectify it. A pseudarthrosis was found and grafts inserted. Progress was slow. the wound suppurated and ten weeks later another operation was decided upon. This time several hydatids were removed. Progress was not satisfactory and destruction of bone so extensive that amputation was advised and performed at the lower third of the thigh after which all went well.

The author quotes Ivanisevich's monograph to the effect that hydatid of bone is always multiple or multilocular. that fractures resulting from their presence may unite but union does not modify the progress of the disease. evolution is slow (5-10 years) diagnosis rarely correct beyond the vague cystic disease of bone. of 464 cases of hydatid operated upon by himself in 2 per cent there was bone localization. prognosis is grave. most of those cases in which a limb is involved require amputation in the end, while spine hydatids are always fatal.

H Harold Scott

PODYAPOLSKAYA, V P & ISAICHEVA, A I [Treatment of Hymenolepidosis with Male Fern in combination with other Preparations.] *Med Parasit & Parasitic Dis* Moscow 1944 v 13 No 5 3-6 [In Russian.]

The authors gave ethereal extract of male fern by the method described by PODYAPOLSKAYA and VASILKOVA (*Med Parasit & Parasitic Dis* 1934 v 3 257) and by other Russian authors. The full dose of male fern is given in three parts on three occasions called cycles with intervals of 10-12 days between them. On the first occasion the treatment lasts two days while the second and third last one day each. In the present series a purgative was given on the evening before the male fern and another followed the male fern. By this method using male fern alone PODYAPOLSKAYA and VASILKOVA (*loc cit* above) obtained 21.7 per cent of complete and constant cures. GOLUBIATNIKOV (*Soviet Medicine* 1942 v 6 26) used two variants of this method and obtained

STEPHENSON R W Treatment of Bilharzias with Stilbamidine. [Correspondence] *Trans Roy Soc Trop Med & Hyg* 1945 Mar v 38 No. 4 306-8

[July 1945]

Nine patients heavily infested with *Schistosoma haematobium* were treated with stilbamidine 15 intravenous injections being given with doses similar to those used by HICK and SART (this Bulletin 1941 v 38 290 1-2 mgm. per kgm. were given daily or on alternate days, the usual total dosage being 2-2.2 gm. The results were judged solely by the effect on the eggs, a cure being presumed when they failed to hatch. In five cases there was no change in the number of eggs in the urine was much reduced but living eggs were still present and two patients were apparently cured. In one of the cured cases no eggs were found in the urine during an observation period of one month after one course of 15 injections. In the second cured case where infestation was very heavy there were very few eggs in the urine at the end of a course of injections though some were living. A second course of 10 injections was given and after the third injection no living eggs were found over an observation period of two months.

The author concludes that the action of stilbamidine is too uncertain to justify its routine use in urinary schistosomiasis.

BERCOVITZ, Z. T., SHWACHMAN H & RODRIGUEZ MOJICA, R. The Blood Picture in Asymptomatic *Schistosoma mansoni* and other Intestinal Parasitic Infections. *Amer J Trop Med* 1945 Jan. v 25 No 1 41-5 1 chart. J F Corson.

In a previous paper BERCOVITZ and others (this Bulletin 1945 v 42, 47) reported changes in the rectal mucosa in 155 Army recruits of Porto Rico who were infested with *Schistosoma mansoni* but had no symptoms of the disease. In the present paper the results of examination of the blood of 147 of these recruits are given. Most of them (130) were also infested with various intestinal worms.

The blood examination consisted of total and differential counts of the corpuscles and estimation of the haemoglobin. In some of the men there was a slight increase above normal in the eosinophile leucocyte count and some showed slight leucocytosis but otherwise the blood findings closely resembled those of a control group of 450 healthy males of Porto Rico. J F Corson

MEIRA, J. A. S. RAMOS J Jr Considerações sobre o electro-cardiograma na esquistossomose mansoni Contribuição para o estudo da miocardite esquistossomótica. Concomitância do forma cardíaca do moléstia do Chagas com esquistossomose mansoni avançada no mesmo doente. [The Electrocardiogram in *Schistosoma mansoni* Infection.] Reprinted from Hospital S Paulo 1944 Nov 717-49 8 figs. [23 refs.] English summary.

The authors studied the electrocardiogram in 20 patients who were infested with *Schistosoma mansoni* but they obtained no results to indicate the presence of myocarditis. The study was complicated by the presence of other pathological conditions in at least some of the patients. From a review of the subject however they concluded that two kinds of myocarditis may occur in schistosomiasis: one very rare is characterized by the presence of schistosomal granuloma in the myocardium, while the other commoner but not yet known, is confused with Fiedler's myocarditis but should be distinguished from it. J F Corson

CASTRO G J Hidatidosis ósea [Hydatid Disease of Bone.] *Rev Med de Chile* 1944 Dec. v 72 No 12 1074-7, 1 fig

The author records two cases of hydatid disease of the tibia in his own practice and adds comments on the condition based largely on a monograph on the subject by Professor Oscar IVANISEVICH of Buenos Aires. The histories are in many respects similar in the two cases—diagnosis is usually delayed and at first erroneous—hence it may be well to present them fairly fully.

The first patient was a man of 25 years who 15 years before had been operated upon for hydatid of the liver. This seems to have been entirely overlooked when he was admitted in 1935 with a fracture of the right leg at the junction of the upper and middle thirds of the tibia. It was put up in plaster of Paris but after 60 days there was no union and the plaster was re-applied for 80 days. Still there was no consolidation but a pseudarthrosis. In view of a doubtfully positive Kahn reaction he was given antisyphilitic treatment without benefit. Radiograms then showed several clear areas in the bone varying in size without periosteal reaction of local sclerosis. Operation was performed and several hydatids removed. The tibia was reduced to a mere shell. He left hospital with a plaster splint and did not return—all that is known of his subsequent history is that he died of pneumonia about a year later.

The second patient was a professor 48 years of age who came to the hospital in June 1944. Four years before when walking he fell and broke his left leg at the junction of the upper and middle thirds of the tibia. A plaster splint was applied. This was removed after 45 days and he was told to rest the limb and have it massaged. He suffered more or less continuously afterwards from pain and could only get along with crutches. He again went to hospital—mal union was diagnosed and operation was undertaken to rectify it. A pseudarthrosis was found and grafts inserted. Progress was slow—the wound suppurated and ten weeks later another operation was decided upon. This time several hydatids were removed. Progress was not satisfactory and destruction of bone so extensive that amputation was advised and performed at the lower third of the thigh after which all went well.

The author quotes Ivanisevich's monograph to the effect that hydatid of bone is always multiple or multilocular that fractures resulting from their presence may unite but union does not modify the progress of the disease—evolution is slow (5-10 years)—diagnosis rarely correct beyond the vague cystic disease of bone. Of 464 cases of hydatid operated upon by himself in 2 per cent there was bone localization—prognosis is grave—most of those cases in which a limb is involved require amputation in the end while spinal hydatids are always fatal.

H Harold Scott

PODYAPOLSKAYA V P & ISAICHEVA A I [Treatment of Hymenolepidosis with Male Fern in combination with other Preparations.] *Med Parasit & Parasitic Dis* Moscow 1944 v 13 No 5 3-6 [In Russian.]

The authors gave ethereal extract of male fern by the method described by PODYAPOLSKAYA and VASILKOVA (*Med Parasit & Parasitic Dis* 1934 v 3 257) and by other Russian authors. The full dose of male fern is given in three parts on three occasions called cycles with intervals of 10-12 days between them. On the first occasion the treatment lasts two days while the second and third last one day each. In the present series a purgative was given on the evening before the male fern and another followed the male fern. By this method using male fern alone PODYAPOLSKAYA and VASILKOVA (*loc cit* above) obtained 21.7 per cent of complete and constant cures. GOLUBYATNIKOV (*Soviet Medicine* 1942, v 6 26) used two variants of this method and obtained

28.1 and 21 per cent of cures. Using a modification of this method IOMINA [this *Bulletin* 1944 v 41 499] obtained 24.1 per cent. of cures. GORYACHEVA [below] obtained 56.2 per cent. of cures (see also KEVORKOV this *Bulletin* 1944 v 41 498) and GORODILKOVA (*Ascid Parasit. & Parasitic Dis.* 1943 v 12, 72) quoted in the paper here under review obtained only 8 per cent. of cures by this method. In the series here described Podyapolskaya and Isaicheva obtained only 2.8 per cent. of complete cures in 108 children. They ascribe this poor result to the effects of difficult wartime conditions which caused malnutrition and crowding which favoured reinfection.

Dissatisfied with the general results of this method of giving male fern although it is better than giving it in single doses Podyapolskaya and Isaicheva tried supplementing the male fern with either acrichine [also called acraquin and similar to atebirin (mepacrine)] or methylene blue or yatren. Acrichine and methylene blue stain tissues and it was thought that they might be toxic to the cestodes and their cysticercoids. Yatren contains 26-28 per cent. of roline and thus might also be toxic to the cestodes. Further its slight laxative action would tend to prevent retention of the cestodes in the gut mucosae after the male fern had detached them.

The experiments were done with children in Samarkand. Out of 1,626 children aged 3-14 years 479 (29.2 per cent.) were infested. Infestation in different groups varied between 7.7 and 64 per cent. Faecal examinations were done by the method of Fulleborn. Children were adjudged cured when not less than five faecal examinations during two months failed to reveal eggs.

Acrichine, methylene blue and yatren were given once daily by the mouth in the doses shown in Table 2 during the days before or after those on which male fern was given. Acrichine was given on 3 or 5 successive days at the first of the three cycles or on 3 days at the second and third cycles. Methylene blue was given on 3 successive days at all three cycles or only at the second and third and sometimes after the third cycle as well. Yatren on 4 successive days at all three cycles or only at the second and third cycles and sometimes after the third as well. The results are shown in Table 3.

Both yatren and methylene blue gave better results than acrichine. Yatren gave strikingly better results when it was given after male fern (28.3 per cent. of cures in 48 children) than when it was given before male fern (6.5 per cent. of cures in 31 children).

TABLE 2

24-hour doses of preparations in grammes according to age in years

Age, years	3	4	5	6	7	8	12	13	14
Male Fern	0.3	0.6	0.9	0.9	1.2	1.2	1.8	2.1	2.1
richine	0.075	0.1	0.125	0.125	0.15	0.175	—	—	0.225
thylene Blue	0.03	0.04	0.05	0.08	0.07	—	—	—	—
ren	0.15	0.2	0.25	0.3	0.35	0.4	0.6	0.7	—
uber of ren treated	305				2		1		2
							8		3

TABLE 3
Efficiency of the different methods of treatment

Supplementary preparation	No treated	Cured		Not cured		Doubtful		Reinfected	
		No	%	No	%	No	%	No	%
Controls (male fern only)	108	3	2.8	97	91.5	6	5.7	2	1.9
crichino	59	9	15.3	50	84.7	—	—	2	3.4
atren (before male fern)	31	2	6.5	28	90.3	1	3.2	2	6.5
atren (after male fern)	46	13	28.3	27	58.7	6	13.0	1	2.2
thylene Blue before each male fern cycle regularly)	88	16	42.1	19	50.0	3	7.9	2	5.3
Methylene Blue (irregularly and before the second cycle)	33	9	27.3	22	66.7	2	6.1	—	—
Methylene Blue Total cases	71	25	35.2	41	57.7	5	7.0	2	2.8
Grand Total	313	52	16.6	243	77.6	18	5.8	9	2.9

The best results were obtained with methylene blue. Given regularly before each cycle of male fern methylene blue gave 42.1 per cent of cures in 38 children given irregularly before the second cycle of male fern it gave 27.3 per cent of cures in 33 children.

The authors conclude that the best treatment in the present state of knowledge is to give either methylene blue before each cycle of male fern or yatren after each cycle. Combinations of all three of these supplementary compounds should be tried. Under peacetime conditions the percentage of cures obtainable will probably be higher.

G. Lapage

GORIACHEVA L. K. [Comparison of the Efficiency of the Treatment of Hymenolepidosis by Different Methods.] *Med. Parasit. & Parasitic Dis* Moscow 1944 v 13 No 5 7-10 [11 refs.] [In Russian.]

After summarizing some of the literature on this subject the author concludes that there is not sufficient statistical material about the efficacy of treatment with pumpkin seeds that although single doses of male fern evacuate large numbers of *Hymenolepis* their effect is only transient and that the method of PODYAPOLSKAYA and VASILKOVA [above] gives a striking percentage of complete cures.

The author experimented with pumpkin seeds and with male fern given either in single doses or by the method of Podyapolskaya and Vasilkova.

1. Pumpkin seeds (*Cucurbita pepo*)—After removal of the outer skin of the seeds they were chopped up and 150–300 of them were given in food on an empty stomach with a saline purge 1 to 1½ hours later. The treatment was repeated after 10 days. The seeds were given to 23 children aged 6 to 12 years. The number of worms expelled was insignificant and no worms were expelled by five subjects. The eggs reappeared in the faeces of 21 out of the 23 children within two weeks to three months. Absence of eggs from the faeces for eight months indicated cure in the other two.

2. Full doses of male fern given by the method of N. P. KETOVSKOV (*Izvestiya Odesk. Univ. 1930 Feb. No. 5 p. 43*)—The patient was prepared by diet and laxatives on the eve of taking the male fern the next morning on an empty stomach. Half an hour before taking the male fern, the patient drank 1 per cent. solution of sodium bicarbonate and had a saline purge 1 to 1½ hours after the male fern. In all, 78 patients some of whom were children were treated by this method. Parasites were expelled usually in great numbers (1 000 to 3 000 specimens with scolices) and subjective symptoms disappeared as the eggs disappeared from the faeces. The effect was, however, transient eggs being found in the faeces of 54 patients from two weeks to five months after treatment, with reappearance of the symptoms. The patients who were regarded as cured were observed for two years during which time no eggs appeared in their faeces nor did symptoms reappear but repeated doses were necessary to effect a cure. These poor results suggested the trial of other methods.

3. The method of PODTAPOLSKAYA and VASILKOVA (see above)—Patients were prepared in the same way as under 2, but one-third of the total dose of male fern was given on three occasions with intervals of 10 days between these fractional doses. Children were given 0.5 gm. per year of age and adults 6–8 gm. In all, 78 patients were treated. Experience shows that small doses of male fern given in this way remove striking numbers of cestodes (500 to 1 200 with scolices per day) and that the maximal number are expelled on the first day. Examinations were done of 32 patients for 6 months to 1½ years and of 14 patients for 6 months. In the course of 1½ years of such examinations, 18 showed no eggs in their faeces (56.2 per cent.) and these were regarded as cured their symptoms also disappeared. These results confirm other reports in the literature of the efficacy of this method, and the author regards it as the best method at present available. *G. Lapage.*

WHITEHILL, R. & MILLER, M. H. Infestation of the Genito-Urinary Tract by *Strongyloides stercoralis*: a Case Report. *Bull. Johns Hopkins Hosp.* 1944 Sept. v. 75 No. 3 169–74.

The authors record the occurrence of the larvae of *Strongyloides stercoralis* in human urine and refer to a previous report of a case by FORMARA [this *Bulletin* 1923 v. 20 229]. The patient was an unmarried white sailor aged 22, who was admitted to hospital in the South Pacific because of frequency of micturition, nocturia and urgency. Five days before admission, larvae of *S. stercoralis* were found in the sediment of his centrifuged urine. The night before admission he had abdominal cramps and diarrhoea. The abdomen was normal except for slight tenderness of each lower quadrant of the colon. For three years the patient had had lower abdominal discomfort after eating, which was relieved by passage of flatus. He had been in the Navy for 18 months and had been stationed in Michigan, New Caledonia, Idaho, the New Hebrides and Fiji and had been in the South Pacific for ten months before admission to hospital. There was a history of diurnal frequency up to 10 times for as long as the patient

could remember with some urgency especially in the early morning and nocturnal enuresis until the age of 10 and then nocturia twice every night. The patient denied sodomy and pederasty. Apart from prickly heat and fungal infections of the feet and genito-crural regions there were no important physical signs.

There were no eosinophils recorded in the differential white cell count.

Urinary sediment examined daily showed larvae of *S. stercoralis* on four occasions during the first ten days. Five cc. of this urinary sediment were added to an equal quantity of the patient's stool which had previously been found by floatation with zinc sulphate to be free from *Strongyloides* or its eggs. The mixture was then kept at 25-30°C for 48 hours. Numerous larvae and a few gravid females and adult males of *S. stercoralis* were then found in the mixture the finding being confirmed by the parasitologist of a large British Colonial hospital. Numerous stools contained eggs of *Trichuris trichiura* but none of *S. stercoralis*.

A complete urological examination revealed only a small slightly trabeculated area on the posterior wall of the bladder and a few small areas of injection of its mucosa with slight injection of the trigone. The vesical orifice was slightly irregular with a small polyp-like projection at 2 o'clock. There was reduced bladder capacity with high pressure.

The authors think there is sufficient evidence for the conclusion that there was an infection of the genito-urinary tract with *S. stercoralis*. Care was taken to avoid contamination of the urine from the stools. No larvae were found in catheter specimens of urine but their appearance in voided urine was inconstant and the larvae were found in the urine on five separate occasions. The symptoms disappeared with the disappearance of *Strongyloides* after treatment. The origin of the infection was not discovered. The authors refer to reports by various authors of the penetration by the filariform larvae of the bowel wall or perianal skin and their entry into the liver, mesenteric venules, lymphatics and lymph nodes [see this *Bulletin* 1930 v 27 979 1937 v 34 30 1939 v 36 844 1941 v 38 118]. The patient was treated with 0.06 gm. gentian violet given for 14 days in enteric-coated capsules by the mouth after each meal. After a week of this treatment the nocturia, urgency and incontinence disappeared and diurnal frequency was reduced to six times. *Strongyloides* also disappeared from urine examined daily. Urinary sediment was negative and mixtures of urine and stools showed neither *Strongyloides* nor its eggs after 48 hours.

The *Trichuris* was treated while the gentian violet was being given with 0.9 gm. hexylresorcinol by the mouth on two occasions with intervals of 12 days. Three days before the last dose eggs of *Trichuris* were present in the faeces.

The patient was discharged on the last day of treatment with gentian violet free of symptoms. A week later urine and stools were negative as were also cultures of mixed urine and stool. Urological examination then showed no important abnormality and the polypoid projection at the urethral orifice had disappeared. The urine and stools were again negative 3 and 15 days later.

G. Lapage

ROGERS W. P. Studies on the Nature and Properties of the Peritenteric Fluid of *Ascaris lumbricoides*. *Parasitology* 1945 Mar v 36 No. 3/4 211-18 13 figs. [59 refs.]

COOPERHALL, L. T. The Problems of Filariasis. *Southern Med J* 1945 Mar v 38, No 3 186-8.

infection was facilitated. Either larvae or gravid females from the intestine were injected directly into the dogs' muscles or gravid females were injected intravenously or intraperitoneally. This parenteral method of infection was introduced by DOERR and other workers [see DOERR and SCHMIDT this *Bulletin* 1931 v 28, 208]. These earlier workers used larvae expressed from fresh muscle or from gravid females. BERGER and STÄHSLIN (*Zent f Bakt I Abt Orig.*, 1929 v 111: 144) injected gravid females into one masseter of guinea-pigs and obtained infection of the masseter of the other side. Matoff used for the experiments here described larvae born from females kept in normal saline or washed out of the peritoneal, pericardial and pleural cavities of rats and guinea-pigs given massive infections. After washing by centrifugation, these larvae were concentrated into $\frac{1}{2}$ to 1 cc. of normal saline and injected with a small Record syringe directly into the masseter (usually the left) of the dogs. Gravid females were collected from the small intestines of infected rats and guinea-pigs by scraping the mucosa with the back of scalpel; they were then washed in saline and injected in $\frac{1}{2}$ to 1 cc. of saline. Intravenous injections of 15 to 40 females were given to five dogs aged from 2 to 5 years. Intraperitoneal injections of 20 to 50 females were given to five dogs aged $1\frac{1}{2}$ to 3 years. Intramuscular injections (into the masseter usually the left) of 150 or 500 larvae, or 20 to 50 females were given to eight dogs aged $1\frac{1}{2}$ to 15 years. The dogs were examined 21 to 144 days after infection. Tables give details of the larvae found in the diaphragm, tongue, masseter and intercostal muscles of the dogs.

All the dogs showed infection of the muscles. Parenteral infection usually produces a higher degree of muscle infection in adult dogs than peroral infection does. The larvae showed no signs of degeneration or death. The age immunity does not therefore extend to the infection of the muscles by the larvae. In other words the muscles do not offer resistance to the larvae as the alimentary canal (gastric juice) does. Very few larvae injected into the masseters developed. Thus when 200 larvae were injected into the masseter of a dog aged $1\frac{1}{2}$ years only 12 larvae were found there by trichinocopy 30 days later. In other instances when 500 were injected into the masseter only 2 were found there 144 days later and when 150 were injected only 1 was found 44 days later. But when gravid females were injected there was a much denser muscle infection because larvae born naturally or by pressure during the injection are more viable than those washed out of body cavities and possibly others become viable in the mother before she dies. This applies also to intravenous and intraperitoneal injection of gravid females.

G. Lapage

DEFICIENCY DISEASES.

CAYER, D., RUFFIN, J. M. & PERLEWEIG, W. A. The Clinical Significance of Glossitis and Cheilosis in Deficiencies of the B-Complex. *Southern Med. J.* 1945 Feb v 38 No. 2, 111-17 2 figs. & 6 charts. [11 refs.]

By applying these laboratory methods [blood levels and saturation tests] to patients having glossitis or cheilosis, one should be able to measure the levels or degrees of saturation of the various vitamins and thus determine the factor or factors responsible for the clinical picture under consideration. Values were determined for vitamins A, C, B₁, B₂, nicotinic acid and pyridoxine in (a) 28 patients showing definite clinical evidence of a deficiency of the B-complex, (b) "30 ward patients having neither glossitis nor cheilosis" (c) 30 medical students. Values for vitamin A were practically the same in the groups with and without glossitis and cheilosis.

In regard to vitamin C a comparison of the arithmetical means of vitamin levels of the various groups showed no appreciable differences. Although five patients and four students had no measureable C in the blood plasma yet no clinical scurvy was encountered.

No correlation was found between the presence of glossitis and cheilosis and either thiamin or pyridoxine excretion.

Although well below the mean for the student controls still no significant differences were found in the riboflavin excretion of the groups of patients with and without glossitis and cheilosis.

On the other hand patients having either of these signs had excretion levels significantly lower than those of the control patients.

The authors however emphasize the fact that "a patient may have glossitis with a normal nicotinic acid excretion level and conversely a low nicotinic acid level does not predicate a sore tongue a multiple deficiency may be implicated.

The authors believe that a nicotinic acid deficiency is a far more frequent cause of cheilosis than a deficiency of riboflavin [They do not state however whether in their opinion the glossitis and cheilosis of nicotinic acid deficiency differ clinically from the conditions met with in riboflavin deficiency as is believed by other observers.]

H S Stannus

STRYKER G V & HALBEISEN W A with the technical assistance of Lucille LEVENTHAL. Determination of Macrocytic Anaemia as an Aid in Diagnosis of certain Deficiency Dermatoses. *Arch Dermat & Syph* 1945 Feb v 51 No 2, 116-23 2 figs [Numerous refs]

Haematological examinations were carried out in a number of patients exhibiting a variety of undetermined dermatological signs suspected to be suffering from a vitamin B complex deficiency.

The skin lesions are described as an imperfectly symmetrical patchy or diffuse superficial pruritic scaly dry or vesicular erythroderma which may be evanescent or later confluent distributed over the sides of the neck, face front of shoulders and upper part of the chest and axillary folds sometimes also over the extremities. Eleven case reports are given.

The condition resembles contact dermatitis but is differentiated from it by the presence of a macrocytic anaemia the history of dietary deficiency and by the fact that the dermatosis and anaemia clear up under treatment with a crude liver extract.

It is pointed out that the eruption may occur in winter time and in indoor workers but nothing is said about the work.

This condition seen in St Louis appears to resemble that described by P Gross *Arch Dermat & Syph* 1941 v 43 504

H S Stannus

MEDICOTT R W Nicotinic Acid in the Treatment of some Psychiatric Syndromes. *New Zealand Med J* 1945 Feb v 44 No 239 28-33

During the last five years medical men in many countries have slowly come to recognize that a variety of mental states may be associated with a nicotinic acid deficiency. In the majority of cases perhaps the suspicion has been aroused by a history of deficient dietary or of some episode likely to upset metabolism, and the diagnosis has been confirmed by the response to the exhibition of nicotinic acid.

Dr Medlicott reports six cases admitted to a mental hospital in New Zealand which serve very well to demonstrate some of the features to be met with in such cases.

H S Stannus.

ALLISON J. R. The Relation of Hydrochloric Acid and Vitamin B Complex Deficiency in certain Skin Diseases. *Southern Med J* 1945 Apr v 38 No. 4 235-40 8 figs.

Four hundred cases exhibiting a variety of skin conditions thought to be associated with a vitamin B complex deficiency were investigated in regard to gastric hydrochloric acid.

The group was drawn from poorer classes taking a diet of white bread, white grits, polished rice, fat meat and a few vegetables.

All showed some deficiency in acid secretion and all improved on being given hydrochloric acid by mouth together with high vitamin diet, yeast and liver. The author believes that treatment with addition of hydrochloric acid is better than by vitamin B complex alone.

H. S. STANNAIS.

HAEMATOLOGY

TOMLINSON W. J. The Incidence of Sickle-cell Anemia and Sickle Cell Anemia in 3,000 Canal Zone Examinations upon Natives of Central America. *Amer J Med Sci* 1945 Feb. v 209 No 2, 181-8 [18 refs.]

There have been no previous reports of sickle cell anaemia or sicklaemia from the Canal Zone or the Republic of Panama. This paper records the incidence of these conditions in the natives of this region based on routine conservative studies of autopsy cases and hospital admissions and on field studies in villages.

The phenomenon of sickling was elicited by the usual technique of examining sealed wet blood films after 24 and 48 hours. In a total of 3,000 examinations sickled cells were observed in 246 (8.2 per cent.). Analysis of sex distribution showed that sickling was present in 7.2 per cent. of males and 11.35 per cent. of females.

In the routine examinations made on autopsy cases and on patients admitted to hospital for various reasons, of a total of 2,372 sickling was present in 210 cases and in these evidence of sickle cell anaemia was found in 21 representing 10 per cent., or 0.9 per cent. of the group as a whole.

Analysis of the age groups of the autopsy cases indicates that sickling is relatively more frequent below the age of 40.

L. J. DAVIS.

TOMLINSON W. J. & JACOB J. E. Studies of Sickle-Cell Formation in Normal Saline, Plasma, and Sera with Carbonic Anhydrase Inhibitors. *J Lab & Clin Med* 1945 Feb. v 30 No 2, 107-11.

"1. Erythrocytes capable of assuming sickled shapes will do so when resuspended in normal saline, their original plasma or serum or in other compatible plasma or serum, providing they have not been washed more than five times in normal saline.

"2. Multiple washings of the erythrocytes remove some substance, possibly carbonic anhydrase, which is necessary for the phenomenon of sickling.

"3. Zinc acetate or sodium cyanide in concentrations of 1:1,000 when added to oxygenated blood, prohibits sickle-cell formation.

"4. Zinc acetate or sodium cyanide in concentrations of 1:1,000 when added to carbonated blood does not reverse the sickled forms and they do not resume discoid shapes when exposed to air or oxygen."

SCHERER J H & CECIL R C. Congenital Hemolytic Anemia in a Negro
J Lab & Clin Med 1945 Mar v 30 No 3 244-6

The first case of congenital hemolytic anemia to be reported in detail in the Negro race is recorded. Apparently the disease though rare does occur among Negroes. The probability of transmission of the trait through miscegenation is discussed

VENOMS AND ANTIVENENES

RIDLEY H. Snake Venom Ophthalmia. *Brit J Ophthalm* 1944 Nov v 28
 No 11 568-72. [18 refs]

Several of the African colubrids are spitting snakes mostly species of *Naja* but the commonest is *Naja nigricollis* the black-necked cobra (sometimes though wrongly called the Black Mamba). This is up to 6 ft in length. When cornered or attacked it slightly opens its jaws and with a sharp hiss two jets of venom shoot forwards for about two feet and afterwards break up into a spray. This may be repeated and the range of action may be 8 and even 12 feet. Injury to the eye is localized and absorption of venom is slight if any. Recovery is usually complete unless secondary infection results in corneal opacities.

The author records a case in a labourer aged 30 years who received a charge of the venom in his right eye at a distance of 4-5 feet. Pain was considerable the conjunctiva was injected and the corneal surface oedematous and sensation absent. The eye was irrigated with saline and atropine was instilled. Next day chemosis was marked and the lids oedematous the lower half of the cornea was denuded of epithelium and sensation still absent. By the fifth day sensation was returning and fresh but oedematous epithelium covered the cornea. This was detached and a fresh layer formed by the 14th day the surface was normal except for a faint localized opacity and vision was 6/6. This opacity persisted for at least two months. The corneal anaesthesia continued for the first week but there was never any sign of absorption or the usual neurotoxic symptoms associated with colubrine poisoning.

The rest of the paper deals with the usual properties of cobra venom and its uses as an analgesic in tabes neuralgias cancer etc. and the effects of Daboia venom as a styptic with which readers of this *Bulletin* are familiar [See this *Bulletin* 1936 v 33 391-96 399 1937 v 34 645 660-63 1938 v 35 520 523 891 1939 v 36 567 605 1940 v 37 464 515 1941 v 38 660 661].

H Harold Scott

MOHAMMED A H. Notes on the Toxins of Egyptian Scorpions. *Biochem J*
 1944 v 38 No 4 284-5

The author prepared purified toxins of four species of Egyptian scorpions in the following way. The telsons after being separated and dried over calcium chloride were ground with quartz sand and small quantities of decinormal HCl. final extraction was made with this strength of acid and the extracts decanted. The extracts were neutralized with normal caustic soda and after addition of a solution of picric acid the liquid was allowed to stand for 24 hours. The precipitate which formed contained the toxin and was extracted with 80 per cent acetone until all the soluble picrate was removed. Next the toxin was precipitated as hydrochloride centrifuged off washed with dry acetone and ether and kept *in vacuo* over P_2O_5 . The m.l.d for the rat was 25-50 μ g/100 gm body weight.

The toxin gave positive Millon and biuret reactions was precipitated by saturated ammonium sulphate by absolute ethanol and by acetone. It precipitated with picric acid the precipitate disappearing on being heated and reappearing on cooling. The toxins were stable at least for six days, when kept at 0°C. in decinormal HCl, unstable in normal NaOH. At 55°C. in distilled water they lost 90 per cent. of their potency in six days. With 0.5 per cent. formalin toxicity fell nearly to half in 15 days to a half with 1 per cent. and to a third with 5 per cent. formalin. At 55°C. 0.5 per cent. formalin reduced the toxicity to one-tenth in 24 hours with 5 per cent. formalin this took place within an hour. The effect of acetaldehyde was more rapid at 55°C the potency was reduced from 0.03 to 0.08 mgm per 100 gm rat in an hour and in 24 hours was reduced to one-tenth. The species of scorpion examined were *Buthus quinquestratus* *B. leptochelys* *B. aculeicarinatus* and *B. hottentotta minus*. For obtaining venom which was done with the first and last of these the poison gland was stimulated electrically and the venom collected through a capillary tube fitted to the sting. The venom was milky and clotted on standing. The absorption bands of all four toxins were the same 278 mμ, that of the two venoms 262.5 mμ. The absorption band was found to change with change in toxicity.

H. Harold Scott

FADRAIRN D. The Phospholipase of the Venom of the Cottonmouth Moccasin (*Akistrodon piscivorus* L.) *J Biol Chem* 1945 Feb v 157 No 2, 633-44 4 figs. [25 refs.]

ESSEX, H. E. Certain Animal Venoms and their Physiologic Action. *Physiol. Rev* 1945 Jan v 25 No 1 (48-70) [22 refs.]

BOQUET P. Action catalytique du cuivre au cours de l'oxydation des venins de "Vipera aspis" et de "Naja tripudians" et d'une toxine végétale la racine par le peroxyde d'hydrogène. [Catalytic Action of Copper during the Oxidation of certain Venoms and Vegetable Toxins.] *Rev d'Immunologie* Paris, 1940-1941 v 6 No 6 393-403. [39 refs.]

RAMON G., BOQUET P. RICHOU R. NICOL, L. & Mlle DELAUNAY RAMON. Sur la production accélérée des sérums antivenimeux de différentes sortes au moyen des ana venins spécifiques et des substances stimulantes de l'immunité aux conditions—see résultats. [Accelerated Production of Antivenoms by Means of Anavennins.] *Rev d'Immunologie* Paris, 1940-1941 v 6 No 6 353-62. [Numerous refs.]

DERMATOLOGY AND FUNGUS DISEASES.

ORTEGA, A. La lesión inicial experimental de la punta mal del pinto o carate en Cuba. [The Initial Lesion in Pinta Inoculations.] *Rev Sifilografía Leprología y Dermatología*. Marianao Cuba, 1945 Jan. v 2, No 1 5-17 9 figs. [23 refs.] English summary

In an examination of many articles on pinta the author has failed to find any description of the initial lesion of this disease. Some have stated that it begins with maculae (now known as *pruritis*). TELLEZ, in 1899 recorded that he had transmitted it experimentally to 70 out of 84 persons, but he gave no account of any initial lesion.

For his experiments the author used serum taken from two patients in Cuba showing early signs of pinta and injected it diluted 1:10 into the front of the forearms of volunteers as in the method for the Mantoux test. In the first experiments three men were inoculated; in a second series nine more, six of these had suffered from syphilis and had strongly positive Wassermann and Kahn reactions. The nine were inoculated from one of the first three who had shown signs of pinta during two years after being first inoculated himself. One of the syphilitics developed a typical pinta lesion. The incubation period between inoculation and the first sign varied widely between limits of 6 and 61 days. The primary lesion and its evolution are described very fully and illustrated by a series of photographs but tell us little more than did León y Blanco in his account in 1940 [this *Bulletin* 1941 v 38 90]. The first sign is a slightly infiltrated erythematous spot, reddish in colour, the size of a pin's head, which enlarges to a papule with squames, reddish in white subjects, dark violaceous in negroes and half-castes. The squamous epithelium becomes stratified and fissured with a red halo. The whole may become lichenoid or like psoriasis or evolve with an atrophic centre, erythematous and squamous border and pigmented areas. There may be many satellite papules. Itching is usually present and the lesion may be aggravated by scratching. *Spirochaetes* are to be found at least in the first 60 days of the infection. [The author acknowledges that León y Blanco was the first to describe the initial lesion in 1939 and gives as reference the paper by the latter abstracted in this *Bulletin* *ibid.* p. 89 but does not refer to the fuller account in a paper following that one in the same journal *Rev Méd Trop y Parasit Habana*, abstracted in this *Bulletin* 1941 v 38 90].

H. Harold Scott

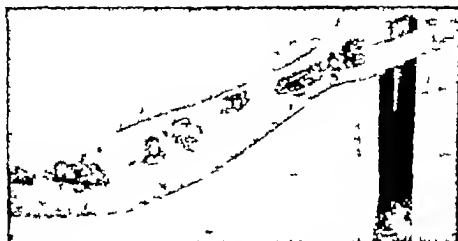
BLANCO F. L. & OTEIZA, A. Sobre la transmisión experimental de la pinta mal del pinto o carate al conejo [Experimental Transmission of Pinta to the Rabbit.] *Salud y Bienestar Municipal Habana Cuba*. 1944 July-Sept v 4 No 1 11-15 4 figs.

Several investigators have tried but ineffectually to transmit the spirochaetes of mal del pinto to laboratory animals; the positive results here recorded therefore are important. In December 1943 a Jamaican negress was seen by one of the authors and diagnosed as a typical case of pinta (the Kahn and Meinicke reactions were markedly positive) and in the cutaneous lesions *Spirochaeta herrejoni* was seen. A volunteer was inoculated in two places on the anterior surface of the left forearm with serum from one of the dyschromic spots and pinta lesions have developed at the site. The next month fluid obtained by pressure from the initial lesions in this volunteer was injected intradermally into the scrotum of each of four rabbits. In June 105 days later one of the rabbits showed a red papule at the site of injection, and ten days later this was topped by a superficial erosion covered by a dark scab. In the blood-stained serum from this numerous spirochaetes were seen and with the fluid four more rabbits were inoculated and also a human volunteer on the left forearm. The latter presented a local inflammatory reaction which disappeared in 72 hours but 18 days after the inoculation there was seen an erythematous spot 2 mm in diameter which in a month increased to 6 by 4 mm and was covered with fine scales; serum pressed from this contained spirochaetes. [See this *Bulletin* 1941 v 38 89 90. It may be noted as of some interest in regard to the original case in the present paper with markedly positive Kahn reaction, that León y Blanco has himself recorded that in primary pinta at least the Wassermann and Kahn reactions are negative (this *Bulletin* 1941 v 38 91) so that the woman was suffering also from syphilis.]

H. Harold Scott

TRESPALACIOS, F., GONZALEZ PERIS G & DE LAOSA O. Esporotricosis linfagítica. Reporte de tres nuevos casos. [Sporotrichial Lymphangitis.] *Rev Sifilografía Leprología y Dermatología* Marianao Cuba. 1945 Jan., v 2, No 1 28-30 3 figs

Sporotrichosis is said to be uncommon in Cuba. the authors consequently deem it worth while to record three cases recently under their care. All three were whites their ages 54 14 and 24 years and all were employed in cane-cutting and sustained slight injuries from cane splinters. In the first the primary lesion was on the upper third of the anterior surface of the left forearm in the



Case of sporotrichial lymphangitis showing primary lesion on the dorsal aspect of the left hand at the root of the thumb and extension along the lymphatics to produce secondary lesions

[Reproduced from the *Revista de Sifilografía Leprología y Dermatología*]

second over the tibio-tarsal articulation of the left foot. In the third on the dorsal aspect of the left hand at the root of the thumb. In each case the evolution was typical early ulceration purulent discharge crusting over and breaking down, and extending along the lymphatics to produce secondary lesions similar to the primary. Administration of iodides gave good results. In the first two *Sporotrichium beermaensis* was cultivated from the third no growth was obtained. H Harold Scott.

NEGRONI P & BONFIGLIOLI H. Piedra blanca de las extremidades de los pelos producida por *Trichosporon riberosi*. [White Piedra of the Hair Tips caused by *Trichosporon riberosi*.] *Rev Argentina Dermatofilologia* 1944 Dec. v 28 No 4 487-94 4 figs.

The authors describe a peculiar type of piedra of the scalp hair affecting only the hair tips. The nodules suggesting the appearance of louse nits were about 1.0 mm. in diameter and consisted of a colony of a hyaline fungus (*Mucedinaceae*) attached tightly to the hair tip, on which it formed a cap or sheath. There was some penetration into the hair substance through the cut end. Microscopically the nodule was found to consist of a densely compacted mycelium breaking up into arthrospores from 3.32 to 4.98 μ in diameter smooth-walled hyaline and tending to become spherical.

In culture the fungus presented the characters of the genus *Trichosporon*. On wort-gelatin the single colony reached a diameter of 5 mm and was elevated cerebriform dry opaque whitish and of a pasty consistency. On liquid media the fungus forms a surface growth. The optimal temperature for vegetation is 25°C to 28°C.

Micromorphology—In parasitic life smooth walled hyaline arthrospores measuring 3.32 by 4.99 μ . In culture a pseudomycelium 1.66 μ in diameter with arthrospores 6.94 to 9.96 μ by 2.50 to 3.30 μ , blastospores 4.50 to 7.62 μ by 3.32 μ and blasto-arthrospores 6.64 to 4.15 μ .

The fungus has no property of fermenting sugar; it coagulates milk but does not liquefy gelatin or coagulated serum.

It was not found pathogenic by intravenous, subcutaneous or intraperitoneal inoculation to the rabbit or guinea pig.

A pure yeast form culture consisting of rounded, oval or elongated cells was developed by repeated subculturing on rabbit blood agar or N N N agar and incubating at 37°C.

A piedra like growth on hairs was produced *in vitro* by sowing the fungus in a medium of gelatin with casein, yeast wort and various salts to which sterilized hairs were added. Nodules developed along the hair shafts but were most numerous at the tip. The growth embraced the circumference of the hair but did not penetrate its substance.

The fungus is described as a new species under the name *Trichosporon ribeiri* Moraes and the diagnosis in Latin is given
J. T. Duncan

SNOW J. S. WADDING E. S. & TOMLINSON W. J. Chromoblastomycosis. Report of the First Case observed in the Canal Zone. *Arch. Dermat. & Syph.* 1945 Feb. v 51 No 2, 90-93 4 figs.

HEAT STROKE AND ALLIED CONDITIONS

WEINER, J. S. The Diuretic Response of Men working in Hot and Humid Conditions. *J. Physiology* 1945 Mar 28 v 103 No 4 36P-37P 1 fig.

Ten men aged 20-25 did physical work by stepping on to a stool one foot high 24 times a minute for 5 minutes in every 20 minutes during two hours. This was done both in ordinary room conditions and in a hot room at 100°F dry bulb 93°F wet bulb (R.H. 77 per cent. eff. temp. 94°F). Immediately before beginning the work each man had a drink of 750 cc. of water and the loss due to sweating was replaced every 20 minutes to preserve the water balance. In the hot room the rectal temperature was about 102°F after two hours and the sweat loss was about 1 litre per hour after the first hour. Sixty-six experiments were made in the hot room and 25 in ordinary room conditions, and the response to 750 cc. of water in ordinary room conditions was studied on 60 occasions. The results were consistent.

In ordinary room conditions diuresis occurred in nearly every case after taking extra water in the morning; about 700 cc. of urine was passed during the exercise period but afterwards very little urine was excreted. In the hot room the urinary output decreased markedly during the two-hour work period; sometimes this decrease did not take place until sweating was profuse. The total amount of urine was nearly always less than half that excreted in ordinary room conditions. A diuresis usually occurred also about an hour after leaving the hot room. The cause of the reduction in the urinary output in the hot room is unknown. Reference is made to experiments by BARCLAY and NUTT (*J. Physiol.* 1944 v 103 20P)
J. F. Corson

PLATT R. Uraemia and Heat-Stroke an Exercise in Diagnosis. [Memoranda.] *Brit Med J* 1945 Mar 31, 445.

The patient referred to in this note was a soldier in Italy who complained of dysuria and frequency of micturition with vomiting. His mental condition was dull, his temperature 101 F. There was heavy albuminuria and the blood urea was 108 mgm. per 100 cc., but there was no haematuria, oedema or hypertension, and the diagnosis of acute nephritis was rejected. It is known that heat stroke can give rise to a similar condition, and this diagnosis was supported by the fact that the patient's knee jerks were absent and that his urine was almost free of chlorides. Rest and the generous administration of fluid and salt led to rapid and complete recovery—the albuminuria disappeared, and the blood urea value was lowered to 20 mgm.

Charles W. Coombs.

TROPICAL ULCER.

MARSH F & WILSON H. A. Tropical Ulcer. *Trans. Roy Soc. Trop Med & Hyg* 1943 Mar v 38, No 4 259-70 [44 refs.]

In December 1942 the authors undertook to investigate and treat cases of tropical ulcer in labourers of the Anglo-Iranian Oil Company in Persia.

In their opinion Vincent's spirochaete and fusiform bacillus are the predominant organisms but dirt and trauma are also essential factors and various causes of ill-health such as malnutrition and infections are predisposing causes. They express the aetiology shortly by the words "Filth Food Friction Fuso-spirilliosis."

A short history of the "lock-up" plaster of Paris method, practised by Whitmet Orr and Trueta for fractures and applied to the treatment of tropical ulcers by COXWELL and BICHARAX (this *Bulletin* 1934 v 31 337) and others, is given, as well as references to nearly all other recent forms of treatment.

The authors used the plaster of Paris bandage over dressings containing various mixtures—nine ointments including "Bipp" and "Zipp" five washes, and potassium permanganate crystals. The composition of these is given in the text and details of cases treated are given in two appendices which lack of space prevented from being printed in this journal; they have been filed, however, at Manson House and are available for reference.

Altogether 85 ulcers were treated—the ulcer was washed and the selected ointment applied on a single layer of gauze, covered with a much larger single layer of vaselined gauze and encased in a plaster of Paris bandage. Patients were seen once a week or once a fortnight. About 70 per cent of ulcers healed within seven weeks—the average time being rather more than two weeks.

The authors concluded that the "lock-up" method is very good that "Bipp" and "Zipp" are valuable applications and that the sprinkling of a fine layer of small potassium permanganate crystals on the ulcer promotes rapid healing in some otherwise resistant cases.

J. F. Corson.

NASALAND PROTECTORATE. ANN REP MED DEPT YEAR ENDING 31ST DEC., 1943 [Abridged]. 12-16. Tropical Ulcer. Dr W. T. C. Barry's Preliminary Review of his Investigations.

This is a preliminary report of a three years' investigation of tropical ulcers in natives of Nasaland. Two villages with very different living conditions were selected and frequent observations were made on leg abrasions occurring in the village children. A detailed report will be given later. During the second

and third years selected groups of children were given dietary supplements—either meat or yeast. In addition to these observations some experiments on volunteers were made.

The author concluded that *fusiform bacilli* played a more important part than *spirochaetes*—no ulcers developed from abrasions infected with cocci only but when *fusiform bacilli* appeared the abrasion became more severe in character. It was observed however that only nine ulcers developed among 120 abrasions in which *fusiform bacilli* were present.

The incidence was much higher in the rainy season than in the dry season in the former there were 10 ulcers in 672 abrasions in the latter five ulcers in 764 abrasions. In the rainy season *fusiform bacilli* were present in 87 (22.8 per cent.) of 381 abrasions in the dry season they were found in only 33 (7.9 per cent.) of 414 abrasions. The difference was attributed to the damp and cold air and also the greater number of flies (chiefly *Musca sorbens*) present during the rainy season.

It was found that ulcers developed among the children who received the meat or yeast supplements.

Experiments on volunteers—Three African labourers were inoculated with ulcer pus on scarified areas over the external malleoli all developed ulcers.

A labourer was inoculated with pus over the external malleolus and also over the external condyle of the humerus on both arms the latter healed by first intention but a typical tropical ulcer developed at the leg site.

Another labourer was inoculated with pus over both external malleoli when ulcers appeared he was kept in bed one leg being raised on a Thomas's splint and the other lowered through a hole in the bed to the ground. After three days the ulcer on the lowered leg was very painful and the leg had to be raised on to the bed the other ulcer was painless and was smaller.

The author inoculated himself and a control with pus from an ulcer [site not stated] the control developed a severe ulcer while the author had only a small sluggishly progressing sore.

In conclusion suggestions are made for further experimental work which is regarded as the most promising method of investigation of tropical ulcers.

J. F. Corson

MISCELLANEOUS DISEASES

MENON I. G. K. Tropical Eosinophilia. *Indian Med Gaz* 1945 Jan v 80 No 1 24-30 [19 refs.]

The author records and analyses eight cases of this curious condition and proceeds to discuss its aetiology. The whole though it does not solve the problem sets forth very clearly the different theories as to its causation and the *pros* and *cons* of each. Even at the risk of repeating what has been said before in this *Bulletin* [1941 v 38 538 539 1943 v 40 720 721 948 1914 v 41 424-426 969] it will be useful to give a resumé of its symptomatology. Males are more often attacked than are females and a common age is 20-30 though cases occur both above and below these limits. There may be a persistent low irregular fever (99-102 F) at the start of illness with dry irritant cough small scattered foci in the lungs or marked hilar shadows both of which may be transient enlargement of liver or spleen may occur but is neither common nor marked there often is loss of weight. Blood changes comprise an increase in red cells as a rule (to 5.3 or even 6.7 millions per cmm.) leucocytes two or three times the normal totals of which eosinophiles constitute one to two-thirds

and are of the mature type. It is not uncommon for the Wassermann and the Kahn (less often) to give false positive reactions. Arsenicals bring about improvement (though the early injections may seem to aggravate the symptoms and some patients get over the acute period of the disease without any treatment).

The question of aetiology is ably discussed under the following heads —

1 *Allergy* —The eosinophilia is in favour but in allergic conditions generally this may not be high and there may be little if any leucocytosis.

2 *Eosinophil leukaemia* —But such a condition is not well established as is myeloid or lymphocytic leukaemia. The prognosis is good whereas in other leukaemias it is bad. In the author's words: "The very existence of eosinophil leukaemia is still under doubt. To postulate the existence of a benign eosinophil leukaemia is therefore only to add to the confusion."

3 *Leukaemoid group* —Lymphadenoma and metastatic malignant deposits are ruled out by the favourable prognosis in tropical eosinophilia.

4 *Infection* —(i) *Helminthic* —No ova seen as a rule. Anthelmintic treatment quite ineffectual in this syndrome even if, ova being present, this element is removed.

(ii) *Protozoal* mentioned but not considered

(iii) *Bacterial or Viral* —The low fever, the splenomegaly and the hepatomegaly (sometimes present) and the transient adenopathy with a progress towards spontaneous recovery are characteristic of other fevers, such as enteric, undulant relapsing fever and infective mononucleosis.

The author concludes that the evidence is in favour of some infection, the nature of which is not yet known.

H Harold Scott

LAL, H. B. Tropical Eosinophilia. A Report on Fifteen Cases. *Indian Med Gaz.* 1945 Jan. v 80 No 1 30-32

[This may be regarded as the counterpart of the last (see MENON above) and it would be of much interest if Colonel Lal and Dr Menon could meet and we could overhear the discussion between them on this subject. The two papers serve to show how opposite opinions can be argued on the same data.] Colonel Lal gives a summary of fifteen cases under his observation. He strongly opposes what he regards as the present complacent attitude of the medical profession in looking upon it as a separate clinical entity which has a specific treatment, namely arsenicals. He sketches the symptoms stating that 12 of the 15 were afebrile [but as MENON states above the fever occurs in the early stages and the present author may have seen his patients after the fever had subsided]. The disease recurs at intervals throughout a long period "one month to ten years." Colonel Lal regards the condition as a sensitization from which the patient has never completely recovered. He may come to the hospital with bronchitis and, after an interval, return with tropical eosinophilia. Variations in symptoms, physical signs and X-ray findings as in asthma, the presence of eosinophil cells in the sputum, lack of permanency of cure: these are the main facts which lead him to regard 'eosinophil lung' as a misnomer and he prefers the name 'allergic pneumonia'.

H Harold Scott

KLOPFSTOCK, A. & STEINRITZ, H. An Epidemic Occurrence of Eosinophilic Erythredema in Palestine. *Harefuah*. Jerusalem. 1945 Mar 15 v 28 No 6 [In Hebrew 117-19 English summary 119-20]

(a) Clinical Aspects

¹ A syndrome previously unknown in Palestine, has made its appearance in Tel Aviv in sporadic cases within the last few years and in large numbers since November 1944.

The characteristic manifestations of this disease are the appearance of red swelling and infiltrations on the skin and mucous membranes which are transient and migrant over wide areas of the body associated with eosinophilia and frequently with leukocytosis.

The etiology is still unknown and till its discovery we tentatively suggest Eosinophilic Erythredema as the name

(b) Epidemiological Aspects

The new syndrome of Eosinophilic Erythredema is characterised by skin swellings and eosinophilia, the latter observable in the blood, sternal punctate and in the tissues. That and the clinical aspect of the disease make it certain that we have to deal with an allergic phenomenon.

More than a hundred cases are known with certainty, but the real number is probably much greater. So far cases were seen in Tel Aviv and its surroundings, Rehovoth, Chederah, Haifa and Jerusalem. The first cases diagnosed were seen in November 1944. Retrospective diagnosis in some cases seems probable as far back as 1942 possibly 1941. It is too early to say anything about the distribution of the disease in the different communities. Neither sex is preferred. Only two cases among children are known so far. As a rule only one member of a family fell ill.

The etiology remains obscure. An extraneous allergen seems improbable. The possibility that the disease could be the allergic phase of Filariasis (Calabar-swelling) is discussed. But no *Microfilaria* have been found, the rare biopsies have yielded no parasites and serological tests could not be performed. Only continued research can bring a solution.

LEFFKOWITZ M & SUKIERNIK S. The Clinical Picture of an Eosinophilic Disease with Cutaneous Manifestations. *Harefnah* Jerusalem. 1945 Mar 15 v 28 No 6 [In Hebrew 120-22. English summary 122.]

The clinical picture of the new disease which made its appearance in Tel Aviv its surroundings and in Jerusalem during the end of 1944 and the beginning of 1945 is described on the basis of 23 cases.

50% of the cases presented prodromal complaints for from 2 to 8 days prior to their illness.

The disease usually starts with severe itching or occasionally only with pain. This is associated with swelling, with or without local heat and redness occasionally in the form of lymphangitis with surrounding redness and infiltration. The swelling usually subsides after 2-3 days but occasionally persists for a week or two. The swelling may appear anywhere and is migratory in character. After it subsides subcutaneous nodules are sometimes found which also disappear after some time. Two cases had enlarged lymph glands and two started with a low grade fever.

While the cutaneous lesions are apparent the patients usually have a feeling of malaise while some continue their occupations as usual.

90% of the cases had an eosinophilia ranging from 8 to 48%, 40% had leukocytosis 11-14 000. The blood sedimentation rate was normal or slightly increased, urine, stools, fluoroscopy of the chest, Kahn, and the red blood count were normal. No parasites were found in thick drops taken both in the day time and at night. Puncture of the swellings showed many eosinophiles and several giant cells.

Etiology is still obscure.

Two days later the patient complained of itching in palms and soles, but there was no rash. When discharged from hospital a week later he still had some alteration of sensation in hands and feet, but no pain.

The remainder of the paper is concerned with general remarks on fish poisoning and quotations from the literature with which readers of this *Bulletin* are familiar.

H. Harold Scott

GENERAL PROTOZOOLOGY

BELTRÁN E. Resultados comparados de diversos metodos para el diagnostico de protozoos intestinales. [Comparison of Diagnostic Methods for Intestinal Protozoa.] *Rev Inst Salubridad y Enfermedades Trop Mexico* 1944 Sept. v 5 No 3 175-84 2 graphs [16 refs.] English summary

The examination of the faeces of 200 children in Mexico for intestinal protozoa by direct examination (saline or iodine) haematovyrin stained films and zinc sulphate concentrations has shown that the first is the most reliable. The examination of three samples by the three methods gave a parasitism rate of 98 per cent. with a 63.5 per cent. rate for *E. histolytica*. The concentration method came second in efficiency. Combination of two methods or all three increases the number of positive results.

C. M. Weyon

BELTRÁN E. & RAÚL LARÉNAS M. Infección humana por *Isospora hominis* en Mexico. [*Isospora hominis* Infection in a Man in Mexico.] *Rev Inst. Salubridad y Enfermedades Trop Mexico* 1944 Sept. v 5 No 3 185-9 2 pls. English summary (4 lines)

The case reported is that of a man 25 years of age suffering from dysenteric symptoms in Mexico City. Faecal examination revealed an *Isospora hominis* infection. This is the first record of this parasite in Mexico.

C. M. Weyon

FREED L. F. Two Cases of *Trichomonas vaginalis* Infestation of the Male. *South African Med J* 1945 Mar 10 v 19 No 5 73

GENERAL ENTOMOLOGY

CALLOT J. & DAO VAN TY. Contribution à l'étude des moustiques français. Culicidés de Richelieu (Indre-et-Loire). [The Mosquitoes of France: Culicidae in Richelieu (Indre-et-Loire).] *Ann Parasit Humaine et Comparée* 1944-1945 v 20 No. 1-2, 43-66 13 figs on 2 pls. [29 refs.]

CULPEPPER, G. H. The Rearing and Maintenance of a Laboratory Colony of the Body Louse. *Amer J Trop Med* 1944 Sept., v 24 No. 5 327-9 3 figs.

The lice are kept on 1½-inch squares of dark-coloured woollen cloth with approximately 100 adult, or proportionately more nymphal lice per piece. The patches with the lice are kept in crystallizing dishes which hold 40 to 60 of them, i.e. 4,000 to 10,000 lice. The lice cannot climb the polished sides of the dishes and escape. The dishes are kept in an incubator at 30° to 32°C. and at about 75 per cent. R.H. Twice a day at 8 a.m. and 5 p.m., the lice are fed on "research subjects." [It is understood that these are usually negroes, employed for the purpose.] The method is as follows: the man having removed his clothes lies face downwards on a table. The cloth squares with the lice are laid carefully all over his back, overlapping like tiles on a roof. The lice leave

the upper side (sometimes they are stimulated to do so by bright light) and begin to feed under the cloth. When they have fed they return to the fabric the whole process taking about 35 to 45 minutes. At the end of the feeding the patches are removed and stray lice are picked off with forceps and finally by rubbing with a towel.

As many as 40 000 lice may be fed, at one time without great discomfort except to sensitive subjects who have to be excluded. The men are very rarely called upon to feed lice more often than once a week. Most of the 40 men employed in this work have fed lice for 6 to 18 months without any apparent deleterious effect on their health.

The method ensures a large and healthy colony of lice. The authors state that they have been using daily about 1 200 lice and 875 eggs in experiments over a period of 18 months.

J R Buxine

OVCHEVNIKOV L. M. [Complex Dusts in Pediculosis Control.] *Med Parasit & Parasitic Dis* Moscow 1944 v 13 No 2 79-83 [In Russian]

OVCHEVNIKOV L. M. [The Use of Albicidal for the Lice Control.] *Med Parasit & Parasitic Dis* Moscow 1944 v 13 No 2 83-7 [In Russian.]

DAVIS L. J. Pulmonary Acariasis in Monkeys. *Brit Med J* 1945 Apr 7 482 1 fig

In view of the possible aetiological connexion between acariasis of the lungs in monkeys and cases of bronchitis asthma and eosinophil lung of obscure causation in man the author records finding mites in the lungs of a Macaque in Hong Kong in 1933. He observed nodules near bronchioles and these nodules were capsular with walls of cellular granulation tissue in the lumen were found the remains of a mite surrounded by cellular detritus. Radiologically small discrete foci were seen scattered in the lungs. There is little doubt that the monkey became infested through inhalation and further investigation may reveal that man suffers similarly from inhalation of dust. [To the unaided eye these foci in monkeys often strongly resemble tuberculous lesions but tubercle bacilli are not seen unless this disease complicates the acariasis. The abstractor when holding the appointment of pathologist to the Zoological Society of London used to send portions of tuberculous organs to the late Stanley Griffith for typing of the bacillus. With a large number of autopsies it was not always possible to examine for tubercle bacilli before sending off the tissues and the reply might be that the tissue was not tuberculous at all but was infested by *Acarus* or that there was a mixture of tuberculosis and pulmonary acariasis. These lesions were most frequently found in the bodies of Rhesus monkeys. See this *Bulletin* 1945 v 42 73]

H Harold Scott

REPORTS SURVEYS AND MISCELLANEOUS PAPERS

CATHIE I. A. B. Tropical Medicine in the Middle East 1940-1942. *Acta Tropica* Basel. 1944 v 1 303-19 1 map

HARRIS P. N. Protection against Lethal Doses of Pentavalent Arsenical and Antimonial Compounds in Rats by *p*-Aminobenzoic Acid, a Histological Study. *J Pharm & Exper Therap* 1944 Nov v 82, No 3 254-60 3 figs

Little work has been done on the histology of poisoning by arsenicals since BROWN and PEARCE [this *Bulletin* 1920 v 15 390] showed that the chief

lesion caused in laboratory animals by trypanamide occurred in the kidney. Recently SANDGROUN and HAMILTON [this *Bulletin* 1944 v 41 372] have shown that PAB (β -aminobenzoic acid) protects rats against lethal doses of trypanamide and stibosan, and does not interfere with trypanocidal action. The present author has studied by histological methods the protective effect of this substance to rats receiving toxic doses of the above drugs. The latter were given to animals weighing 80-100 gm., in a single dose of 3,200 mgm. per kgm. intravenously in the case of trypanamide and in a dose of 250-375 mgm. per kgm. or in some cases two doses of 250 mgm. per kgm. on successive days in the case of stibosan. Some rats were also given PAB in doses of 750-1,000 mgm. per kgm. on 1-5 occasions on successive days the first dose being administered shortly before the arsenical or antimonial (designated as PABA rats the others being the controls). Twenty-four hours after drug administration, the two sets were markedly different in appearance and the difference became more pronounced. The controls were lethargic, their eyes were covered with exudate, and many died. There was some indisposition and a few deaths in the PABA set. When control animals died, a corresponding number of the other set were killed for comparative studies. In rats receiving trypanamide alone renal lesions were most constantly present, only 1 of 11 animals being normal. They consisted of areas of necrosis of varying degree in convoluted tubules with later regeneration occurring in some cases. Other pathological changes were present in heart liver lungs thymus and intestines. The kidneys in 8 of 10 of the PABA rats were normal. The renal lesion was also most prominent after administration of stibosan, and none of 32 rats which received this substance alone had normal kidneys, while 7 of 17 in the PABA set were normal.

J. D. Fulton

[In this paper the letters PABA are used in reference to rats given β -aminobenzoic acid and treated with an arsenical or antimonial, but the same letters have been used by other authors to refer to β -aminobenzoic acid alone. In Spanish the letters APAB (acid β -aminobenzoic) have been used to indicate the acid.—Ed.]

YUDKIN J. A Simple Test for the Detection of Bile Pigments in Urine. [Memoranda.] *Brit Med J* 1945 Mar 31 445.

The author (*Nature* 1945 Jan 13 50 *J Trop Med & Hyg* 1945 v 48 1) as shown that coloured substances, such as mepacrine (atebrin) can conveniently be estimated by "adsorption colorimetry" the substance being adsorbed on to a measured amount of white absorbent powder. In the present paper he describes a simple method for the detection of bile pigments in urine.

To about 10 cc. of urine in a test tube add about 0.25 cc. of silica gel powder (sifted to pass 60 mesh but not 120 or 130 mesh) and swirl the tube round once or twice every 1 or 2 minutes so as to shake the powder in the urine. After 10 minutes allow the powder to settle and pour off the supernatant urine. Add a few cc. of water to the powder again allow it to settle, and pour off the water. A brown coloration of the powder indicates the presence of bile pigments.

The test is eight times as sensitive as Gmelin's nitric acid test and is only slightly less sensitive than the Fouchet test. Silica gel powder already sifted may be obtained from Silica Gel Ltd. Aldwych House London, W.C.2.

J. F. Corson.

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VERTEBRATES AND ARTHROPODS EXAMINED IN INVESTIGATIONS OF THE EPIDEMIOLOGY OF YELLOW FEVER.

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Some animals particularly monkeys and opossums in the South American jungle seem to play an important part in the epidemiology of yellow fever. As the virus can multiply only within cells and as it circulates only for a few days in the blood, owing to the rapid development of specific antibodies it is thought that there can be no animal reservoir of the disease in the sense in which the term is usually employed i.e. a persistent infection of varying degrees of severity from inapparent to acute infections with little risk of its dying out from lack of susceptible animal hosts. In yellow fever infection is so quickly followed by immunity that the term animal reservoir seems to be unsuitable though the difference appears to be one of degree rather than a qualitative one. In some mosquitoes however the virus may persist for some weeks and probably for the lifetime of the insect and it has been suggested that the true reservoir may be said to be the insect vector.

In man and monkeys the presence of antibodies to the virus of yellow fever whether found in nature or developed after experimental inoculation of the virus by the syringe or by mosquito bite is regarded as indicating that the virus has multiplied in the cells of the body and has circulated in the blood even though no illness may have been caused by it. This view is based upon a considerable amount of observation and experiment it applies to both the ordinary (viscerotropic) and the neurotropic viruses and means that the animal was susceptible to infection and became immune. It forms the basis of surveys to discover the extent of areas where yellow fever exists or has existed.

Some individuals of other Orders of vertebrates however have been found to possess naturally-occurring antibodies to yellow fever in places and circumstances where previous infection with yellow fever has been impossible as well as in areas where such infection could not be excluded though apparently very unlikely. These antibodies have usually been called non-specific the animals in which they occur are not necessarily immune to infection with yellow fever since the inoculation of a small dose of the virus stimulates the production of further antibodies which are regarded as specific and as indicating that the virus has multiplied in the body cells and has circulated in the blood. Special care and precautions are therefore necessary for the correct interpretation of the presence of naturally-occurring antibodies to yellow fever in animals other than monkeys. Some animals are resistant to infection and these may or may not have so-called non-specific antibodies in their blood.

It has been shown that yellow fever virus can persist for some time in the bodies of various invertebrates including other arthropods than mosquitoes but

so far as is known at present, the latter are the only vectors in nature. As the virus can pass through the skin and mucous membranes various ways of mechanical infection are possible. It has occurred in several laboratory workers.

The following extract from "The Rockefeller Foundation—A Review for 1944" by Raymond B. Fosdick is of great interest—

"In Villavieja alone in an endemic yellow fever region, more than 2,000 animals have been trapped, ranging all the way from mice to wildcats and monkeys, and from birds to snakes and other reptiles. Each was tested to see whether it had acquired immunity to yellow fever or if not, whether it responded to inoculation with the virus. Two species only showed positive results—the monkey and the opossum. That is antibodies against yellow fever were found in their bloodstreams evidence that at some time past they had been infected with the virus.

In June 1944 the laboratory at Ilhéus trapped a rock monkey, a marmoset. In its bloodstream were discovered not antibodies but the active virus of yellow fever. The animal was seriously ill and soon died, and exhaustive laboratory tests showed conclusively that it had died of yellow fever.

"This episode is historically interesting because it is the first time in any country that a wild animal has been picked up in its natural habitat suffering from yellow fever. It lends support to the thesis that yellow fever is primarily a disease of jungle animals transmitted by jungle mosquitoes."

In the accompanying Table I of animals tested for susceptibility to yellow fever virus infection is indicated by a plus sign and negative results of experiments by a zero sign. a note of interrogation indicates a doubtful result. Susceptibility has been shown by illness (with death or recovery), pathological lesions, the presence of circulating virus, or the presence of specific antibodies. Infection has been produced by the bites of naturally or experimentally infected mosquitoes, by injection of emulsions of ground-up bodies of mosquitoes, and by injection of infected blood or tissue by various routes, including the intracerebral route. The presence or absence of naturally occurring antibodies in the blood is also recorded in this table but except in monkeys these antibodies should not be regarded as specific without consulting the original papers. A short list of invertebrates in which the virus can persist for various periods is given in Table II.

The presence of yellow fever virus has been demonstrated in wild-caught mosquitoes and in mosquitoes allowed to feed, under laboratory conditions, on infective animals. Two methods have been used, (1) to allow the mosquitoes to feed on a clean susceptible animal, in which cases a positive infection is due to virus transmitted by bite, and (2) to inject into susceptible animals an emulsion of the triturated bodies of a pool of mosquitoes, in which case a positive result indicates only the presence of virus in the bodies of mosquitoes. The significance of the retention of virus in the bodies of mosquitoes which have failed to transmit the infection by biting is doubtful. Of the wild-caught mosquitoes (not given a further opportunity of becoming infected after capture) the only species proved infective by bite are *Aedes leucocelaenus* and *Haemagogus capricornis janthinensis equinus*? but the presence of virus has been proved, by injection of triturated mosquito bodies in wild-caught *Aedes aegypti* and *Aedes simpsoni* and in a pool of 58 *Sabethine* mosquitoes of various genera. Except in the case of the fatal infection of LAZEAR in a hospital ward where mosquitoes were being fed on yellow fever patients, and where the origin of the mosquito which bit him was unknown, no wild-caught *Aedes aegypti* appears to have been directly proved infective by biting; the circumstantial evidence however is conclusive. Details of the findings in mosquitoes infected under laboratory conditions are given in Table III.

TABLE 1*—VERTEBRATES TESTED FOR SUSCEPTIBILITY TO YELLOW FEVER VIRUS.

Species	Common Name	Country	Viscerotropic				Neurotropic			References <i>Tropical Diseases Bulletin</i> Year and page
			Mosq		Inj Bld or Tiss	Inj Bld	Neurotropic			
			B	I			IC	EC		
CLASS MAMMALIA										
ORDER PRIMATES										
FAMILY PONGIDAE										
<i>Gorilla gorilla</i>	Gorilla	Africa								1939 632 1942, 65
<i>Pan satyrus</i> [<i>Australopithecus troglodites</i>]	Chimpanzee				+				+	1928 537 339 1932, 576, 1936 339 1939 632 634 1941 432
<i>Pan satyrus schweinfurthi</i>	Chimpanzee								0	1936, 339 1939 632 1942, 65
FAMILY CERCOPITHECIDAE										
<i>Cercopithecus adolphi</i>	African grey monkey		+		+			+	+	1929 851 1930, 483 1938 124
<i>C. [C.] griseiventris</i>	Tantalus monkey		+		+					1940 83 1943 771
<i>C. tentans</i>	Diana monkey								+	1930 875 1931 719 1933 354 1936 624
<i>C. diana diana</i>	Dark green monkey								+	1938, 124
<i>C. nigroviridis</i> [<i>Alouatta palliata</i> nigroviridis]	Green monkey				+			+	0	1936, 339
<i>C. adolphi adolphi</i> [<i>C. callitrichus</i> or <i>Lasiopyga callitrichus</i>]	Patas or Howler monkey		+		+			+	0	1934 (579) 1935 550 1936 339
<i>C. felax</i> [<i>Erythrocebus felax</i>]	Mountained guenon				+			+	0	1930 875 1931 719 1936 624
<i>C. cephus</i>	Schlegel's guenon								0	1936 339
<i>C. neglectus</i>	Malbrouck's guenon								0	1936 339
<i>C. adolphi cynosurus</i>	Mona monkey				0			+	0	1939 632
<i>C. mona</i>	Lowe's mona monkey		0						0	1930 875 1931 719 1936 624
<i>C. mona lowei</i>	Schmidt's white monkey								0	1936 339
<i>C. ascensis schmidti</i>	monkey	(Gold Coast)							+	1942 455
<i>C. sp.</i>									0	1938 124

* NOTES.—Mosq = mosquito. B = transmission by bites. I = transmission by injection of crushed bodies. Inj Bld or Tiss = injection of blood or tissues of infected vertebrate. I.C. = intracerebral injection of virus. E.C. = extracerebral injection of virus. P.A. = protective antibodies. The references are to abstracts in the *Tropical Diseases Bulletin*. See also *Hindus* table in this Bulletin 1933 v 30 285.

[illegible]

ORDER LIPOTYPHILA

FAMILY ENIMACHIDAE

Echinococcus europaeus

E. prunellae [E. albidiventris]

E

FAMILY SOCIETY

Crocodermis marmorata

ORDER. RODENTIA FAMILY SCURIDAE <i>Sturnus vulgaris</i>	Europe	(visc.)	+	1934 498
<i>Sturnus asiaticus</i> <i>Eutamias erythrops</i>	S. America	0	0	1939 652
	Africa	0	0	1936 339
<i>Citellus citellus</i>	Europe and Asia	0	0	1938 497
FAMILY CAVIINAE <i>Cavia porcellus</i>				
<i>C. endonatus</i>	S. America	+	+	1930 488 1931, 291 1932 (579)
<i>C. aperea (profusca?)</i>				1934 498 1941 434
<i>Hydrochatus hydrochatus hydrochatus</i> FAMILY CUSCUTIDAE <i>Cuscuta paca</i>	Pig-livcavy or Erlebeben's guinea pig	+	+	1941 434 1939 652
	Capybara	+	+	1939 652
<i>Dasyprocta aguti</i> <i>D. vestigialis</i>	Lapa or spotted paca	+	+	1941 434
	Golden agouti	0	0	1934 81 1939 652
<i>Coendou prehensilis</i> FAMILY HYSTRICIDAE <i>Athysanella africana</i> [<i>Athysanella africana</i>]	Variegated agouti	+	+	1941 434
	Brazilian tree porcupine	0	0	1939 652
<i>Athysanella africana</i> [<i>Athysanella africana</i>] FAMILY MURIDAE <i>A. podiceps</i>	Bush-tailed porcupine			1939 652 1944 122
<i>A. podiceps</i> <i>A. podiceps</i>	Long-tailed field mouse or wood mouse	0	0	1934 498
	Striped mouse	0	0	1936 339
<i>A. podiceps</i> [<i>A. podiceps</i>] <i>A. podiceps</i>	Striped mouse	0	0	1936 339
	Field rat	0	0	1938 125
<i>A. podiceps</i> <i>A. podiceps</i>	Pouched rat	0	0	1938 339
	Golden hamster	0	0	1934 498 1938 125 1939 497 1939 652
<i>A. podiceps</i> <i>A. podiceps</i>	Bank vole	0	0	1934 498
<i>A. podiceps</i> <i>A. podiceps</i>	Short tailed vole or grass vole	+	+	1934 498
	Mouse	+	+	1933 353 1939 652
<i>A. podiceps</i> <i>A. podiceps</i>	Mouse	+	+	1933 353 1939 652

ORDER ACCIPITRIFORMES																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																										
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TABLE II.—INVERTEBRATES IN WHICH YELLOW FEVER VIRUS (VIRUS TROPICUS) HAS BEEN SHOWN TO PERISH

Species	Common Name	Period	References <i>Tropical Diseases Bulletin</i> year and page
<i>Blatt germanica</i>	Cockroach	15 days	1925 638
<i>B. orientalis</i>	Cockroach	under 2	1942, 68
<i>Schistocerca gregaria</i>	Desert locust	under 2	1942, 63
<i>Locusta migratoria migratoria</i>	Locust	under 2	1942, 63
<i>Hemidebora maculata</i>	Leach	8	1942, 63
<i>Agrilus agratus</i>	Slug	under 2	1942, 63

TABLE III.—BLOOD-SUCKING ARTHROPODS TRANSMISSION EXPERIMENTS

Species	Country	Caught in nature		Infected in laboratory		References <i>Tropical Diseases Bulletin</i> year and page
		Between	in	Between	in	
<i>Aedes aegypti</i>	Africa		+	+		1932, 198 1933 6 1939 25
<i>A. aegypti</i> var. <i>quarandensis</i>	"			+		1942, 688
<i>A. (Stegomyia) fuscus</i>	"			+	+	1929 1005
<i>A. albopictus</i>	Asia			+	+	1930 486
<i>A. excrucians</i>	S. America	0				1945 114
<i>A. apicimaculatus</i>	Africa			0	0	1929 848
<i>A. boninensis</i>	S. America	0				1945 114
<i>A. fuscus</i>		0	0	+	+	1931 727 1934 77 1935, 490 1939 23 1945 114
<i>A. fulvithorax</i>				0	+	1932, 197 1933, 490
<i>A. fulvus</i>		0	0			1930 27
<i>A. gambiae</i>	France			+	+	1938 117 1939 636
<i>A. triseriatus</i>	Africa			0	+	1933 353
<i>A. triseriatus</i>	S. America	+	+			1939 27 1942, 634
<i>A. triseriatus</i>						1945 114
<i>A. triseriatus</i>	Africa			+		1929 848 1942, 72
<i>A. metallicus</i>				+		1943, 602
<i>A. metallicus</i>				+		1940 832 1942, 683
<i>A. nigricapillus</i>				0	+	1943 602
<i>A. nubilus</i>	S. America			0	+	1933 353
<i>A. podopneustes</i>	"	0				1945 114
<i>A. punctipennis</i>	Africa			0	+	1933 353
<i>A. scutellaris</i>	S. America	0	0	+	+	1930 484 1934 77
<i>A. variegatus (A. scutellaris)</i>	Asia			+		1936 490 1939 25 27
<i>A. variegatus</i>	S. America	0	0	0	+	1930 484 1932 197
<i>A. variegatus</i>				0		1939 27 1945 114
<i>A. variegatus</i>				0		1945 114
<i>A. variegatus</i>	Africa	+	+	+		1929 1005 1941 431
<i>A. variegatus</i>				+		1942, 759 1943 602
<i>A. variegatus</i>	S. America			+	+	1933, 848
<i>A. variegatus</i>				+	+	1930 484, 1931 727
<i>A. variegatus</i>				+	+	1938, 490 1939 25
<i>A. variegatus</i>	Africa			+		1942, 686 1943 602
<i>A. variegatus</i>	S. America	0	0	0	+	1932, 197 1933 490
<i>A. variegatus</i>				+	+	1939 27
<i>A. variegatus</i>				+	+	1939 639

*Transmission experiments were made by allowing the mosquitoes to bite a susceptible animal or by injecting an emulsion of their ground-up bodies into the animals. Both wild mosquitoes, as caught and mosquitoes experimentally fed on an infected man or animal were used.

J. F. G.

Species	Country	Caught in nature		Infected in laboratory		References <i>Tropical Diseases Bulletin</i> year and page
		Bite	Inj.	Bite	Inj.	
<i>A vittatus</i>	Africa			+	+	1929 1005 1940 532
<i>A whitmorei</i>	S America		0			1945 114
<i>Eretmapodites chrysogaster</i>	Africa			+	+	1928 848 1941 431
<i>Psorophora albipes</i> (Luttrell)	S America	0	0			1939 27 1945 114
<i>P cingulata</i>				+		1932 197 1939 25
<i>P ferax</i>		0	0	+	+	1932 197 1938 490
<i>Haemagogus capricorni</i> * (<i>H janthinomys</i> <i>H equinus</i> ?)		+	+	+	+	1939 25 27 1945 114 1938 491 1939 27 1942, 684 1944 475 1945 114
<i>H urialet</i>				0	+	1938 491
<i>H lucifer</i>			0?			1945 114
<i>Wyeomyia bromeliarum</i>				0	0	1931 727
<i>W obdita</i>				0	0	1931 727
<i>W sp</i>			0			1931 727 1945 114
<i>Dendromyia</i> sp			0			1945 114
<i>Limatus durhami</i>			0	0	0	1931 727 1945 114
<i>Sabethes</i> sp. (3 species)		0	0			1939 27
<i>Joblotia digitata</i> [<i>Trichoprosopon digitata</i>]				0	0	1932 197 1933 5
<i>Joblotia</i> spp [<i>Trichoprosopon</i> spp]			0			1945 114
<i>Sabethoides serratoria</i>			0			1945 114
<i>Sabethoides</i> sp			0			1945 114
<i>Sabethoides Limatus Wyeomyia Goridia Trichoprosopon</i> —20 species 88 specimens		0	+			1939 27
<i>Culex fatigans</i>				+	+	1932, 197 1934 487 1939 25 1941 431
<i>C nigripalpus</i>	S America			+	+	1938 490
<i>C thelasius</i>	Africa			+	+	1933 4 353 1941 431
<i>Taeniorhynchus titillans</i>	S America			+	+	1933 5 1939 25
<i>T albicosta</i>				0	+	1932 197 1938 490
<i>T (Alansonoides) africanus</i>	Africa			+	+	1930 483 1941 431
<i>T chrysomotum</i>	S America			0	+	1932, 197 1938 490 1939 25
<i>T fasciolatus</i>				0	+	1932, 197 1938 490 1939 25
<i>T justiamansonii</i>				0	+	1938 490
<i>T unifornis</i>	Africa			0	+	1933 4
<i>Anopheles albivittatus</i>				0	0	1932, 197
<i>A gambiae</i>				0	0	1930 483
<i>A farsimaculatus</i>	S America			0	0	1932, 197
<i>Phlebotomus</i> sp.			0			1945 114
<i>Glossina morsitans</i>	Africa			0		1942, 65
<i>Stomoxys calcitrans</i>	S America			+	+	1935 294
<i>Amblyomma cajennense</i>				+	+	1934 80
<i>Argas persicus</i>				0	+	1934 80
<i>Boophilus microplus</i>				0	+	1934 80
<i>Ornithodoros moubata</i>	Africa			0		1934 80
<i>O rostratus</i>	S America			+		1934 80
<i>Rhipicephalus sanguineus</i>			0?	+		1934 80
<i>Cimex lectularius</i>				+		1930 483 1931 292
<i>C hemiptera</i>				0		1930 483 1933 5
<i>Triatoma magista</i>				+		1931 727 1933 353
<i>Ctenocephalus canis</i>				0	+	1935 284

Edwards (*Genera Insectorum* Diptera Culicidae Edwards 1932) ruled *H equinus* (= *H capricorni*). Dr Noave Director of the Imperial Institute of Entomology has kindly given me the following information—"Most authorities treat *Haemagogus equinus* and *H capricorni* as distinct species, with *janthinomys* as a synonym of the latter. The status of *apogonini* Brethton, is doubtful. Dyer 1921 treated it as a synonym of *capricorni* but Lane 1939 places it amongst his "*incertae sedis*." Cerqueira [this Bulletin 1944 v 41 782] regards it as a valid species with *janthinomys* as a synonym.

SUMMARY OF RECENT ABSTRACTS *

VII. HELMINTHIASIS

General

BURROWS (p. 408) has made a study of the intestinal parasites of the inmates of a mental hospital in South Carolina. The main point is that both the frequency and intensity of infestation in these patients increase with length of residence. Even among the attendants those who deal with the more deteriorated patients show higher infestations than the others.

Trematodes

LUTTERMOSER and PIFANO (p. 590) have found eggs of *Schistosoma mansoni* in 78 per cent. of the inhabitants of one area of Venezuela. Here the conditions are optimum for the development of snails in the rivers which are much used by the people. Measures of control are suggested, which include destruction of snails with lime when the soil is acid, or with copper sulphate or carbonate the breeding of ducks and cleansing of waterways. Education the raising of standards of agriculture and treatment are other measures projected or advised. LUTTERMOSER (p. 592) states that infestation with *S. mansoni* has been found in 20 per cent. of autopsies at the Vargas hospital in Venezuela in recent years. He reports that snails, miracidia and cercariae can be killed by lime which does not harm the cattle and is a useful antibacterial agent.

In studying the course of experimental infection of mice with *S. mansoni* MAYER and PIFANO (p. 591) have found that the worms are most likely to pass large numbers of eggs a short time after they have reached maturity—probably in man, at about the time when dysenteric symptoms are likely to occur 4-5 weeks after first infestation. In later stages tissue reactions in the gut tend to obstruct the passage of eggs. The authors discuss infestations in which few or no eggs are passed, and conclude that these may be due to schistosomes predominantly of one sex. It has been shown that the cercariae which escape from a single snail are very often of one sex only and it seems quite possible that man may acquire an infection confined to worms of one sex. Some degeneration of liver cells occurs in unsexual infestations, which may be due to immature worms and may be the basis of cirrhosis. (Cott (this Bulletin 1923 v. 20 220) suggests the view that sex in the schistosomes is differentiated in the miracidium, and that a snail infected by one miracidium or by more than one all of the same sex will produce cercariae of one sex only.)

TRIM (p. 299) emphasizes the toxic symptoms which may be found in infections with *S. mansoni* but which are not often seen in Africans. These may include high fever and there may be diarrhoea and acute abdominal pain, as in a case he describes. Another useful sign is the presence of discrete rubbery glands in the groin.

GILBERT (p. 299) in a contribution on schistosomiasis of the female genital tract and neighbouring tissues makes the point that in all his cases (in S. Rhodesia) the infection has been due to *S. haematobium*. Fibrotic reaction is very great and often renders surgical procedures difficult. The urinary tract of course is commonly involved, but there have been a few recorded cases of ovarian disease and the vagina is not uncommonly attacked. The

*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1944 v. 41. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

uterus is not often affected but may contain schistosome eggs. There may be papillomatous masses in and around the vulva. Infestation usually occurs early in life. Surgical treatment is often needed since drug treatment though necessary cannot affect already formed fibrous tissue.

DI PRISCO (p 946) discusses the possibility that certain dermatoses—neurodermatitis, chronic prurigo and a form of pruritus—may be caused by infection with *S. mansoni*.

PLAZA IZQUIERDO (p 677) maintains that in Venezuela Banti's disease is almost always due to *S. mansoni*, the infestation being mainly or perhaps entirely due to male worms. The parasites are not however found in the spleen, the enlargement of which is due to perisplenitis, infarction or portal obstruction. Splenectomy may give good results.

OTTOLINA and ATENCIO (p 945) take the view that the methods used in Venezuela and elsewhere for the diagnosis of *S. mansoni* infection fail in a very large proportion of cases. They therefore attempted biopsy of liver and searched for eggs after the specimen had been subjected to a simple digestion treatment. There is however a risk of haemorrhage in this procedure and the authors therefore took biopsy specimens from the rectum. They found that these were always positive when the liver was positive and that eggs were more numerous in the rectum than in the liver tissues. Rectal biopsy revealed 11 infections in 100 persons whose stools had been negative for eggs and was also positive in certain patients thought to be cured after courses of tartar emetic. Biopsy is a simple and rapid procedure and it is probable that if multiple biopsy were performed, a still higher incidence of infection would be revealed. It could be used to supplement skin and complement fixation tests.

PIFANO and MAYER (p 589) have investigated the Fairley complement fixation test in infections with *Schistosoma mansoni*: the hepatopancreas of infected snails was used as a source of antigen. The reaction was positive in a few cases as early as the beginning of the third week after contact with infested water, later when the disease was established, it was positive in 97 per cent of cases and in the late stages the reactions were strongly positive. The test is therefore valuable. It permits the diagnosis of a trematode infection and points to infection with a schistosome but the fact that it is occasionally negative in proved cases of schistosomiasis *mansoni* shows that it cannot be relied upon completely to exclude that disease.

The NATIONAL RESEARCH COUNCIL of the United States (p 222) have issued a summary of current literature on anthelmintic which though used in several diseases is particularly valuable in schistosomiasis.

GOODWIN and PAGE (p 222) have investigated the excretion of the catechol portion of the Stibophen (Fouadin) molecule. This is quicker than excretion of the antimony portion. The function of catechol appears to be to keep the circulating antimony in solution in a non toxic form while it is being absorbed by the liver or excreted by the kidney.

GELFAND and OSBURN (p 137) describe katayama, a syndrome which may occur in schistosomiasis and which is well recognized in Japan and Egypt. It usually begins 4-6 weeks after exposure to infected water and consists of irregular fever, urticaria and eosinophilia. Several cases have been seen in S. Africa. The authors point out that there may be considerable difficulty in diagnosis.

LI and CHIEN (p. 56) report a case of chronic intussusception of the caecum into the colon, associated with the presence of eggs of *Schistosoma japonicum* and ulceration of the mucosa. They think that the eggs caused the ulceration and that this led to local spasm and to intussusception.

SEIDAT (p 57) discusses *Cercaria ocellata*, a cause of schistosome dermatitis in man. He concludes that several species are included under this name and

describes three other cercariae from *Lymnaea palustris* and several from other snails. He points out that spread of cercarial dermatitis in open bathing places in European big towns is to be expected as the urbanization of wild aquatic birds (ducks, gulls, swans) increases. Most of the 11 species of schistosomes found in Europe are parasites of birds.

MACFARLANE (p. 847) has investigated swimmers' itch in New Zealand. Three types of lesion are found—macules in those not previously infected, papules in those who have previously been attacked and (in one case) macules with pruritic oedema. There was some evidence of immunity in persons previously infected, and this was sometimes local in areas of thick skin. On the other hand, general immunity was shown by some who had never been infested. The parasite is closely related to *Cercaria dios* and *C. ocellata* but appears to be a new species and is named *C. longicauda*. It penetrates the Malpighian layer of the skin, but does not pass into the dermis. In 75 hours after infection biopsy specimens show that all traces of the cercariae have disappeared. Several snail hosts have been found; the vertebrate hosts are probably ducks.

NEGHME and OSSANDON (p. 300) report a case of human infection by *Fasciola hepatica* in which one fluke was found in the subcutaneous tissue over the right eighth rib three weeks after operation for gall stones and in which the presence of another in the liver was inferred because eggs continued to be passed in the faeces. *F. hepatica* has not often been found in man, and the authors refer to the literature on the subject in which some 150 cases are recorded. Ectopic localization of the flukes is much more rare. The condition of the patient now reported improved after a course of emetine injections.

VALDÉS DAPIEXA and PÉREZ HURTADO (p. 1052) give an account of a case of infestation with *F. hepatica* in which the patient had daily fever with rigors and pain and tenderness in the right hypochondrium. No parasites were found in the faeces but eggs of *F. hepatica* were present in bile obtained by duodenal intubation.

MORREAS (p. 677) reports infection with *Fasciola hepatica* in several members of two families in the Roume region of France and suspected infection in others. He tested these families, and a series of controls, with a scratch test and an intradermal test, in which the antigen was prepared from fresh flukes obtained from cattle. The results were suggestive but positive reactions were given by some of the controls.

LAURENT *et al.* (p. 760) report two more cases of infestation with *Fasciola hepatica* in Tunisia. They point out the danger of eating cress from unknown sources and advise that in suspected cases bile obtained by duodenal intubation should be examined.

MILLER and WILBUR (p. 497) report seven cases of paragonimiasis in members of the United States forces who have been in Samoa and the Solomon Islands. The clinical features included persistent cough, pain in the chest and expectoration of sticky, colourless sputum containing brown flecks. Only one patient had haemoptysis.

CAMEROX (p. 781) has given an account of the morphology, taxonomy and life history of *Metorchis conjunctus*, a trematode which has been found in man and other animals. The intermediate hosts are snails and a fresh water fish. This trematode is found widely in Canada, especially in mink and red fox. Details should be sought in the original abstract.

Cestodes.

VOX BOVSODORFF (p. 583) in his investigations of the relationship between *Diphyllobothrium latum* and pernicious anaemia has shown that the worm contains a substance capable of inhibiting the activity of the protease of gastric juice which is active at pH 5 to 8 and above and which is supposed to be the

so-called intrinsic factor. He (p 594) points out that the proteolytic gastric enzyme active at neutral reaction is present in *D latum* anaemia as it is in cryptogenic pernicious anaemia. The same author (p 594) shows that after expulsion of the worm in infected persons with pernicious anaemia, there is usually a definite reticulocyte response and blood regeneration. In these cases the anaemia is due to the parasite but in other cases the association is only accidental.

The same author (p 678) has shown that, if patients harbouring *D latum* are maintained on a diet poor in the extrinsic factor of Castle the removal of the worm does not lead to increase of reticulocytes or of red cells. If however substances rich in this factor are added to the diet there is a strong reticulocytosis and improvement in the blood values. The intrinsic factor was evidently present in these cases.

TÖTTERMAN (p 858) has shown that the Price-Jones curve in tapeworm anaemia [presumably due to *D latum* infection] agrees exactly with that of cryptogenic pernicious anaemia.

HIRVONEN (p 594) has made a study of the serum iron in cases of infestation with *D latum* and *Taenia saginata*. The details should be sought in the original abstract.

DE MEILLON and LEECH (p 301) report a case of sparganosis from Uganda. The sparganum was found in one of several small nodules in the connective tissue round the spermatic cord during an operation for inguinal hernia. The species of the worm was not determined. The authors suggest that sparganosis may be more common in Africa than the meagreness of reported cases suggests in general the majority of recorded cases are from the Far East.

DUGUID and SHEPPARD (p 857) describe an epidemic in trout (in S Wales) due to plerocercoids of a tapeworm belonging to the Diphyllbothridae. The worm was not definitely identified and there is some discussion as to whether or not it was *D latum*. HICKEY and HARRIS (p 858) note that trout from reservoirs near Dublin are infested with plerocercoids the matter is being investigated.

PODYAPOLSKAYA (p 301) has found that a method of examination which involves taking scrapings from the perianal folds (as in the diagnosis of *Enterobius* infections) is a more accurate means than faecal examination for detecting the presence of *Taenia saginata*. The value of this method depends upon the fact that when the segments of the worm move they leave behind a trail of eggs; the scrape method therefore depends upon the characteristic crawling habit of *T saginata* and does not apply to infestations with *T solium*. Faecal examination is more efficient in detecting infestations with *Trichuris*, *Ascaris* and *Hymenolepis*.

GAERTGENS (p 138) discusses the serological diagnosis of *Taenia* infections. These are not useful in tapeworm infections of the intestine but are valuable in echinococcosis. In suspected cysticercosis important diagnostic aid may be obtained from the examination of blood and cerebrospinal fluid by complement fixation and precipitin methods. antigen is prepared from pig cysticerci. Flocculation tests are also useful. Sera of patients with cysticercosis may also react with *Echinococcus* antigen but differentiation is possible by the kaolin adsorption technique.

PRIOR (p 58) reports a case of cerebral cysticercosis in a man who had no previous history of epilepsy but who passed into the condition of status epilepticus during an attack of pneumonia and died. The cysts were not disintegrated or calcified, and the author thinks that under the influence of the acute systemic disease they probably imbibed fluid and became tense thus causing symptoms. BERNALES and ENCINAS (p 58) describe a case in which many cysticerci were found in the ponto-cerebellar area and in which

there were signs of lesions of various cranial nerves, the cerebellum, pyramidal tracts and finally signs of bulbar compression.

HOLMAN and PIERSON (p. 782) do not regard as reliable either the intradermal or the complement fixation test for hydatid disease. They point out also that the disease may be present for years and that organs may be extensively involved, before symptoms are caused. They quote three cases to illustrate these points.

GRASA (p. 764) has found that in the serum of patients with hydatid cysts who have been given subcutaneous injections of hydatid fluid there is a great increase of haemolysins and agglutinins for sheep red cells. It seems that previous sensitization of the tissues is necessary for the production of these heterophilic antibodies which appear to be of a new type.

KEVORKOV (p. 498) has considered the possibility that man may become infested with *Hymenolepis murina* of the rat, and thinks that this is possible in spite of the fact that in Russia there is little coincident infestation with *Hymenolepis* of man and rodents though it does occur in some parts. He (p. 498) notes that tens or even hundreds of thousands of *Hymenolepis nana* may be found in a human patient, especially if the patient is a child. He discusses treatment and concludes that this should be given only if there are symptoms. Male fern is used, but should preferably be given by a fractional method. IOTIVA (p. 499) does not regard treatment of *Hymenolepis* infestation with male fern by the standard methods as efficient. A new method is needed.

LARSH (p. 764) has succeeded in inducing a degree of immunity against *Hymenolepis nana* var *fraterna* in mice by intraperitoneal injection of fresh worm antigen. This immunity is transmitted by artificially immunized female mice to their young and in them is not as high as in mice suckled by mothers with actual infestation with the living worms.

LARSH (p. 765) has studied in mice the relationship between splenectomy and resistance to infection with *Hymenolepis nana* var *fraterna*. Details are given in the original abstract.

Charles Wilcocks

[To be continued]

MALARIA.

BRITISH GUIANA Report of the Malaria Investigations Service of the Medical Department, British Guiana, for the Year 1943 [BEVIER, G. Director Malaria Research Unit 103 cyclostyled pp 2 charts.

The almost complete disappearance of *A. darlingi*, the only known vector of malaria in the coastal belt of British Guiana consequent upon the prolonged drought of 1938-1941 has been described in previous reports [this Bulletin 1943 v 40 512]. In December 1942 nearly 40 inches of rain fell and another 80 inches during the first half of 1943 the latter being 28.60 inches above the sixty year average for these six months. *A. darlingi* became very prevalent and the incidence of malaria abnormally high, epidemic in places. The morbidity returns of medical districts and estate hospitals indicate the east to west march of infection or spread of *A. darlingi*.

The results of spleen and parasite surveys of school children in different parts of the colony are reported in detail.

East Bank Berbice Estuary July 1943.—Spleen rate 57.3 parasite rate 70.0 *P. falciparum* 94.7 *P. vivax* 13.3 *P. malariae* 4.7 per cent. of positive slides in the remainder identification was doubtful. East Indians had higher spleen rates and larger spleens but lower parasite rates than had Negroes. This was a general observation.

East Bank Demerara Estuary July 1943—Spleen rate 37.3 parasite rate 41.9 *P. falciparum* 45.5 *P. vivax* 28.5 *P. malariae* 7.3 per cent of positive slides remainder doubtful

West Bank Demerara Estuary September–October 1943—Spleen rate 58.5 parasite rate 48.9 *P. falciparum* 38.4 *P. vivax* 31.2 *P. malariae* 2.7 per cent of positive slides

West Coast Demerara October 1943—Spleen rate 14.6 parasite rate 22.0 rates indicative of malaria of recent introduction.

The spleen and parasite rates in Georgetown City are referred to in another report (see below)

The total number of anophelines captured during 1943 was 12 768 of which *A. darlingi* were 96.05 per cent *A. tarsimaculatus* 2.59 *A. albiparvus* 0.71 and *A. triannulatus* 0.65 per cent. In the drought years 1940 and 1941 *A. tarsimaculatus* had been as numerous as *A. darlingi*. *A. albiparvus* when disturbed in grass or bushes near its breeding grounds may attack during the day. *A. triannulatus* prefers the blood of mules and cows to that of man. *A. tarsimaculatus* is more likely to be taken in evening than in morning catches and it prefers animal to human bait: this species was not only relatively but actually less numerous in 1943 than it had been in the drought years. *A. tarsimaculatus* may consist of more than one species: its preference for breeding in salt waters may explain its greater prevalence in drought years. *A. darlingi* shows a decided preference for human blood. It is more frequent in morning than in evening captures: it enters dwellings during several evening hours and seldom leaves before the day is well advanced. Where it has been established for some time the seasons of its maximum prevalence are from December to March and from July to September.

Most surface waters along the coast of British Guiana are artificial—canals, drainage ditches, rice fields, flooded cane fields, ponds and borrow pits. The exceptionally heavy rain in the first half of 1943 changed the usual characteristics of surface waters: the black water usually characteristic of canals was absent, the saline content which had been so high during drought years fell to normal. During the year observations were made on 11 199 ground water collections for the presence of larvae, saline content, reaction and other characteristics. In all 21 467 larvae were identified. A large amount of information was obtained regarding the breeding habits of *Anopheles*: *A. darlingi* in particular. Acid and brackish waters are not favoured by this species. A field laboratory has been opened in which these observations can be continued and extended under controlled conditions.

Dr JARDINE, the medical officer of the Demerara Bauxite Company at Mackenzie, 65 miles up the Demerara River, reports a gradual increase in the number of malaria cases since 1942. Anophelines have also increased since 1941, particularly *A. darlingi*. Among anopheline larvae found *A. triannulatus* is most abundant. *A. darlingi* comes second, about 20 per cent. *A. apicimaculatus*, *A. kompi* and another species which do not occur on the coast are found at Mackenzie.

An ecological study of the vegetation of flood fallows on ten sugar estates along the coastal portion of British Guiana was carried out by D. B. FANSHAWE; his report is included.

Norman White

GIGLIOLI, G. *Malaria in the City of Georgetown and its Suburbs*. 54 cyclo-styled pp. 1 plan. [C.O. Ref. No. 60286/45 dated 23rd March 1945.]

This is a very comprehensive malaria survey report of the City of Georgetown, British Guiana: it records the results of observations carried out over a number of years. Some of these years were very abnormal. Deficient rainfall amounting

to drought occurred from September 1933 to June 1941. The year 1943 had a record high rainfall of 122 inches.

Georgetown lies on the Atlantic Coast on the right bank of the Demerara River estuary. The municipal area covers 2½ square miles and has a population of about 73 000. The adjacent suburbs to the east and south-east harbour about 12,000 people. Thus the urban and suburban population combined is almost a quarter of the total population of British Guiana. For the eleven year period, 1933-1943 the average vital statistical rates for the municipal area were: birth rate 28.1, death rate 18.7, infant mortality rate 106.

The only vector of malaria in British Guiana is *A. darlingi*. There are no suitable breeding places for this mosquito within the city proper. In the suburbs however and in adjacent sections of certain city wards malaria is endemic or hyperendemic. From September 1940 to November 1942, *A. darlingi* completely disappeared from the Georgetown area as a result of the drought. In the early part of the drought parasites were still to be found in a large proportion of children in certain areas and *P. malariae* infections were most in evidence. By the end of 1943 *A. darlingi* had become once more very prevalent: it was breeding in abundance all round the city. The incidence of malaria in some suburban areas reached epidemic proportions, probably because of the loss of immunity during the healthy drought years. Gametocyte carriers were abnormally numerous. At this time 1,377 children were examined in the suburbs and adjacent city areas: the spleen rate was 29.3, the parasite rate 48.1 and the gametocyte rate was 10.4 per cent. In the worst area a parasite rate of 82.3 per cent. was found. By August 1944 the epidemic had spent itself and the severe endemicity of pre-drought years prevailed once more.

The malaria problem is very serious in the southern suburbs and wards of the city. The chief breeding sites of *A. darlingi* are nearly all outside the inhabited fringe: notably in Le Repentir Cemetery and in rice grounds and cane fields. The author believes that breeding in the cemetery might be controlled by flooding its whole drainage system with sea water. The eggs of *A. darlingi* die in water containing more than 6 gm. NaCl per litre: in water containing up to 3 gm. per litre *A. darlingi* may develop normally. The water in the estuary which receives the effluent from the Cemetery has a saline content of from 20 to 25 gm. per litre in the dry weather and from 8 to 12 gm. in the rainy season.

The breeding in rice grounds and cane fields will be more difficult to control. Intermittent flooding of the former so that they never contain water for more than six consecutive days might succeed.

In the eastern suburbs and adjacent city wards malaria is not so severe as in the south, but the multiplicity of breeding places in these semi-rural settlements complicates control measures. Irrigation in the north-eastern suburbs is from a canal with water of high acidity. The acidity decreases on standing and by dilution with rain water and conditions quickly become favourable for *A. darlingi* breeding. Should it be possible to retain the acidity of the irrigation water by controlled drainage and more frequent intake less breeding would probably take place.

Spray killing of adult mosquitoes with the new insecticides in houses on the fringe of the city might give important results. The habits of *A. darlingi* render it very vulnerable to such a form of attack.

During the first eight months of 1944 all but one of the 3,377 adult anophelines captured in houses in the Georgetown area were *A. darlingi*. The solitary exception was *A. tritaenatus*. The Yellow Fever Service in 95 routine inspections of trains coming in from the East coast collected 41 *A. darlingi*, 820 *A. tritaenatus*, 43 *A. albipennis* and 3 *A. triaxatus*. All four species breed in profusion in the Georgetown area, but *A. darlingi* alone frequents human habitations.

In the parasite survey of 1,377 children carried out from December 1943 to February 1944 malaria parasites were found in 866 or 48.1 per cent. The species were *P. vivax* 199 *P. falciparum* 251 *P. malariae* 11 226 ring forms of doubtful identity 18 double infections and two triple infections. Gametocytes were found in 51.8 per cent. of the *P. falciparum* positive slides. The low incidence of *P. malariae* is in striking contrast to the findings in the same areas in the drought year 1940 when *P. malariae* was found in 85 per cent of all positive slides.

Norman White

TRINIDAD GOVERNMENT ROCKEFELLER FOUNDATION Malaria. Annual Report, 1943, of the Co-operative Work in Trinidad and Tobago, B.W.I. pp vii+70 numerous figs. sketch maps & photos. 1944 Govt Printers.

A malaria survey report of Trinidad and Tobago was summarized in this *Bulletin* 1944 v 41 445. The present report carries the story still further and details the work carried out in 1943.

The Government malariologist (H. P. S. GILLETTE) reports on school surveys the slide diagnostic service treatment centres and field and control activities. Eighty-four schools in scattered areas were examined 9,987 children were examined for splenomegaly and 4,800 blood slides were examined. The malaria incidence was lower in 1943 than in 1942. Very remarkable results have been obtained in the Toco area in the County of St. David in the north of the Island of Trinidad by attention to the prolific breeding of *A. aquasalis* in water dammed up in blocked river mouths during the dry season. What was an area of hyperendemicity now shows spleen and parasite rates of low endemicity. In three schools the spleen rates in 1941 were 81.5 72.0 and 71.1 in 1943 these rates had fallen to 12.1 8.3 and 20.8. Formerly parasite rates were higher than spleen rates in 1943 the reverse was the case. In one school the parasite rate had fallen from 81.6 per cent. to nil.

The slide diagnostic service is of great value to practitioners and provides interesting information concerning the prevalence of malaria in different parts of the colony. During the nine months in which the service was in operation 14,117 slides were received. Malaria parasites were found in 5,524 72.9 per cent. *P. falciparum* 23.7 per cent *P. vivax* 2.1 per cent *P. malariae* and 1.2 per cent mixed infections. *P. vivax* infections were most in evidence in April and May.

R. C. SHANNON describes investigations on *A. aquasalis* during the year. Most of the villages bordering on the Caroni and Laventille swamps have very low malaria rates in spite of the enormous quantities of *A. aquasalis* breeding throughout most of the year. The low malaria rates are attributed in large part to the strongly zoophilic disposition of the species. In a large buffalo stable near one of these villages tens of thousands of *A. aquasalis* may be found nightly. In two other villages where domestic animals are few high spleen indexes have been noted. In these villages there appears to be a significant correlation between the ratio of animals to man and the spleen rates. Donkeys and probably mules and horses are as attractive to *A. aquasalis* as are buffaloes and cows. Some interesting details are given concerning the trapping of *A. aquasalis* in an animal baited dawn trap the construction of which is illustrated. *A. aquasalis* has two dominant tendencies to enter stables and houses at night to feed and to depart from buildings at dawn. Experiments are being made as to the possibility of reducing malaria in certain villages by means of these traps. With regard to the breeding of *A. aquasalis* it was found that floatage is essential for heavy breeding and that the pH of the water had little influence. It has been found breeding in waters with a pH of 3.7 and of 8.0.

In the wetter portions of Trinidad *A. bellator* is responsible for the high incidence of malaria on cacao estates. It breeds in bromeliads which parasitize

immortelles the shade trees, on the plantations. A discussion of the bromeliads and the bromeliad-anophelines by C. S. PITRENDRIGH occupies about a third of the space in this annual report. Ecological studies have been continued. Some experiments were begun with a heavy spraying equipment (the Gypsy Moth Sprayer) using a copper sulphate solution, to destroy bromeliads. No bromeliads were too high for the equipment to reach and they were destroyed, but some damage was done to cacao leaves. Further experimental work is necessary. One species of bromeliad alone *Grassia aquilegia* supports almost all the *A. bellator* of cacao estates. Selective hand removal of this species may be economically possible. Owing to the present slump in the cacao industry in Trinidad the trees in a large part of the island have been practically abandoned. A replanting scheme is being considered by the Agricultural Department. It might be possible to dispense with shade trees. Cacao has been profitably grown elsewhere without the use of other trees for shading. A joint committee of the Agricultural and Health Departments and the Rockefeller Foundation is considering the matter.

NORMAN WATTS

JASWANT SINGH & JACOB V. P. Malaria Investigations in North Kanara.
J. Malaria Inst. of India 1944 June v 5 No. 3 287-303 2 charts &
 2 maps. [14 refs.]

This is a record of a year's observations in the North Kanara District the southernmost district of the Bombay Presidency with a coastline on the Arabian Sea of about 75 miles. The district lies between 13° 15' and 15° 32' N. and between 74° 7' and 75° 10' E. There is a coastal strip from 3 to 10 miles in width which is crossed by four rivers which form estuaries and numerous back waters along the coast. Eastward the coastal strip merges into the foothills some 10 to 15 miles in width and some 200 feet above sea level. To the east again hills attain a height up to 2,500 feet—they are covered with evergreen forest and perennial streams flow through narrow winding valleys. Still further inland the upland area becomes open and flat. The climate is equable, with no extremes of heat or cold—the seasons are not well marked except the rainy season. The average rainfall is 107.5 inches of which 90.5 inches fall during June, July and August, the south-west monsoon. The population is 441,000.

In most of the coastal belt there is but little endemic malaria, spleen rates under 5 per cent. being the rule. In the foothills malaria is severely endemic, hyper-endemic in places. Spleen rates of 80 per cent. and over were recorded in several villages. In the interior of the district malaria is generally hyper-endemic with but few exceptions.

Two parasite surveys were carried out, 1,890 and 1,587 children being examined. They disclosed parasite rates of 21.6 and 17.8 per cent. respectively. *P. malariae* is the most prevalent species of parasite 53.2 and 63.7 per cent. of positive findings in the two surveys. The remainder were *P. vivax* and *P. falciparum* infections the former being slightly more numerous than the latter. Transmission may occur during any month but is less active from July to September than at other times.

The following species of *Anopheles* were identified—

<i>A. fluviatilis</i>	<i>A. tessellatus</i>	<i>A. maculatus</i>
<i>A. culicifacies</i>	<i>A. annularis</i>	<i>A. stephensi</i>
<i>A. jeyporensis</i>	<i>A. hyrcanus</i>	<i>A. theobaldi</i>
<i>A. pallidus</i>	<i>A. varuna</i>	<i>A. turkui</i>
<i>A. subpictus</i>	<i>A. barbrostris</i>	<i>A. cruciformis</i>
<i>A. vagus</i>	<i>A. philippinensis</i>	<i>A. aethiops</i>
<i>A. jamaica</i>	<i>A. splendens</i>	<i>A. insulariflorum</i>
<i>A. karnari</i>	<i>A. leucosphyrus</i>	

A. fluviatilis was the only species incriminated as a vector. It was never found in large numbers either as a larva or as an adult. It favours human dwellings as resting places. Slow running streams with marginal vegetation are preferred as breeding places but occasional breeding takes place in a variety of places but always in close proximity to human habitations. Of 88 engorged females 56 contained human blood and 32 the blood of cattle. Of 897 specimens dissected oöcysts or sporozoites were found in 99 an infection rate of 11 per cent. *A. fluviatilis* is rare in the coastal belt a fact that accounts for the low malaria endemicity there.

A. culicifacies which MHASKAR (1915) had reported to be the malaria vector in North Kanara does not appear to play any important rôle. Eight hundred and twelve were dissected without any evidence of infection. Precipitin tests on 48 specimens gave positive results in 42 all cattle blood.

Of 255 *A. annularis* dissected none was infected.

Spray killing of adult mosquitoes should prove of value in the control of malaria in North Kanara.

Norman White

ABRAHAM A C & SAMUELS R D. Epidemiology of Malaria in the Nizamsagar Aynot Area, Nizamabad District, Hyderabad State. *J. Malaria Inst. of India* 1944 June v 5 No 3 305-18 1 map & 2 graphs.

The Nizamsagar Irrigation Project was completed in 1933. A masonry dam two miles long was built across the valley of the river Manjra, forming a reservoir with an area of 50 square miles. A main canal 98 miles long with 1100 miles of distributaries can irrigate 275 000 acres of land. Water is supplied throughout the year there are two crops of rice annually. The advent of irrigation led to increased malaria incidence for which inadequate drainage faulty construction and inadequate maintenance seepage and borrow pits have been responsible.

Adult anophelines captured and identified numbered 57,281 —

<i>A. subpictus</i>	33 727	<i>A. lessellatus</i>	51
<i>A. annularis</i>	16 947	<i>A. barbirostris</i>	33
<i>A. culicifacies</i>	3 184	<i>A. jayakeri</i>	21
<i>A. hyrcanus</i>	1 004	<i>A. stephensi</i>	8
<i>A. fluviatilis</i>	984	<i>A. splendidus</i>	8
<i>A. aconitus</i>	943	<i>A. theobaldi</i>	5
<i>A. vagus</i>	217	<i>A. turkhanus</i>	2
<i>A. pallidus</i>	137		

The chief malaria vector is believed to be *A. fluviatilis* but of 177 dissected only one was found infected. It was found breeding extensively in the canal distributaries and the smaller channels as well as in rainwater pools and seepages. *A. culicifacies* probably plays some part in malaria transmission of 1 442 dissected none was infected.

The spleen rate of 1 145 children examined between September and January was 43.8 per cent. Male children had higher spleen rates than females they wear fewer clothes.

Parasites were found in 396 of 865 slides examined 45.8 per cent. *P. malariae* 153 *P. vivax* 119 *P. falciparum* 101 mixed infections 23.

Malaria is least prevalent during the months of heaviest rainfall June and July. The numbers of *A. fluviatilis* and *A. culicifacies* captured during May, June and July were lower than in any other months.

A malaria control scheme was put into operation in 1942 the results have been encouraging. The spray killing of adult mosquitoes the use of oil and of paris green as larvicides, minor engineering works the stocking of selected mosquito breeding places with *Gambusia* and prophylactic administration of quinine in certain hyperendemic villages are the measures employed.

Norman White

JACOB M & SWAROOP S Degree of Accuracy realized in Malaria Forecasts in the Punjab for the Years 1923 to 1942. *Indian Med Gaz.* 1944 June v 79 No. 6 282-9

— & — The Forecasting of Epidemic Malaria in the Punjab. *J Malaria Inst. of India* 1944 June v 5 No. 3 319-35 1 map.

The low-lying plains of the Punjab which are liable to inundation as the result of abnormally heavy monsoon rainfall and the consequent overflow of rivers and stormwater channels have been afflicted by widespread epidemics of malaria at intervals sometimes of many years. GILL [this *Bulletin* 1923 v 23 753] described a method of forecasting such epidemic manifestations of malaria, and his method has been used continuously ever since. In these papers a statistical evaluation of the accuracy of these forecasts supports the conclusion that malaria epidemics in the Punjab can be predicted with considerable precision.

The forecasts are issued at the end of August or beginning of September and relate to the events of the subsequent months. October is the month with the maximum mortality from fever in the Punjab. The factors favouring epidemic manifestations of malaria in any locality are: marked excess of July-August rainfall over the normal, or extensive floods; an epidemic potential above 60; a relatively low spleen rate in June compared with previous years; and conditions of scarcity during the preceding year as reflected by the high cost of staple foods. The epidemic potential factor indicates the relative liability of districts to epidemic visitations. The standard deviation of deaths from "fevers" during the month of October in each district was multiplied by 100 and the product divided by the number of years that had been taken into account (33 years). Where the epidemic potential is very low no appreciable epidemic is likely to occur; if it be over 60 an intense epidemic might occur.

For expressing the intensity of an epidemic an index called the epidemic figure is worked out. The average monthly fever deaths during October-November and December of any year are divided by the mean monthly fever mortality figure for the four months April to July of the same year. Regional malaria epidemics in the Punjab occur exclusively in the autumn. This epidemic figure is based solely on malaria mortality; malaria morbidity figures are unobtainable. The index is therefore, not a wholly reliable index of malaria incidence.

[Though the contention that accurate predictions are possible may be conceded, their very accuracy seems to show that they have served but a very limited useful purpose: otherwise they could have been falsified more often by appropriate action.]

Norman White

RAO G. R. Malaria in the Jharia Mining Settlement, Bihar. Parts II, III & IV [Abstract.] *J Malaria Inst. of India* 1944 Dec v 5 No. 4 471

RUSTOMJEE, K. J. Observations upon the Epidemiology of Malaria in Ceylon. [Abstract.] *J Malaria Inst. of India* 1944 Dec v 5 No. 4 468-70

FAUST E. C., SCOTT J. A. & McDANIEL G. E. Malaria Mortality and Morbidity in the United States for the Year 1943. *J National Malaria Soc* Tallahassee Fla. 1945 Mar v 4 No. 1 66-76 [19 refs.]

This report is based on information supplied by the bureau of vital statistics of all the States of the United States regarding deaths attributed to malaria. Morbidity statistics are also included but these for the most part are necessarily very incomplete. The malaria mortality rates for the United States as a whole and for the malarious south-eastern States are the lowest on record. The total number of malaria deaths was 622, 0.47 per 100,000. Of these deaths 92.6 per cent. were reported from the Southern States. In Mississippi and North

It will be seen that the temperature in April has a more pronounced influence than that of the preceding September and the author suggests that this influence is best explained by the circumstance that when the weather is cold in April the people remain longer exposed to the bites of infected overwintering mosquitoes than when April is warmer. It is also suggested that the findings are inconsistent with the view that the spring peak of incidence is explained by the occurrence of a prolonged incubation period following infection acquired in the previous autumn.

Graphs are reproduced to show the remarkable decline in the incidence of malaria in Sweden and Finland. Since 1910 the number of cases in any year has been negligible in Sweden, where, up to 1881 the yearly number of cases usually ranged from 4 000 to 8 000.

In Finland it is believed that in 1820 no less than 1,044 persons died of the disease: the total population at that time was 1 177,500. The only considerable epidemic in recent times in Finland was in 1902 when 3,300 cases were registered. In each of the years 1920 and 1921 there were about 500 cases; otherwise since 1910 the disease has been almost non-existent.

The decline in both countries is attributed to improved economic and cultural conditions: no great change has occurred in the degree of human association with cattle and other domestic animals.

The only vector mosquito found in Finland is *Anopheles maculipennis* (typicus and messasi according to EABLOM *Bull Soc Path Exot* 1938 v 31 647) which occurs all over the country. *John W D Meigs*

MOSEKOVSKI S D [Quantitative Laws of Malaria Epidemiology Sixth Communication. The Dynamics of Malarimetric Values. Part I.] *Med. Parasit & Parasitic Dis.* Moscow 1944 v 13, No 4 3-25 21 figs. [In Russian.]

SERGIEV P G & TIBURAKAYA A [The Peculiarities of Strains in *P. vivax*] *Med. Parasit & Parasitic Dis.* Moscow 1944 v 13 No 5 38-47 2 figs. [In Russian.]

The authors compare two strains of *P. vivax*: one isolated in Nakhichevan, in southern Russia (the Southern strain) the other from Moscow province (the Northern strain). Parasite counts made at different periods of the infection in 32 patients who were divided into two groups experimentally infected with the Southern (17) and Northern (15) strains respectively showed that these strains differed considerably in the number of parasites produced in the course of the infection. In the case of the Northern strain the mean number of parasites per count was 478.9 (1 604,370 parasites in 335 counts) whereas the mean number in the Southern strain was 186.6 (609,990 parasites in 359 counts). Thus the average number of parasites per count in the first-named strain was 2.5 times as great as in the last named. This points to a higher antigenicity of the latter strain as compared with the former.

The authors also compared the gametocyte productivity and the infection rate in mosquitoes fed on patients infected with the two strains of malaria. The mean number of gametocytes per 500 leucocytes was 8.9 (33-5.9%) in the case of the Northern strain and 14.5 (67%-7.8%) in the case of the Southern one. The number of sexual forms produced by the latter thus being 1.5 times as great as that by the former.

A total of 959 mosquitoes were fed on patients: 62 of whom were infected with the "Southern" strain and 47 with the "Northern" one. In the former case 46.7 per cent. of the mosquitoes became infected, in the latter 19.1 per cent.

the results thus corresponding to the number of gametocytes present in these strains. The two strains also differed with regard to their response to treatment with quinine the Northern strain being more resistant than the Southern one but there was no difference in their reaction to acridine [mepacrine]

C A Hoare

BENNISON B E & COATNEY G R. Inactivation of Malarial Parasites by X-Rays *Pub Health Rep Wash* 1945 Feb 2 v 60 No 5 127-32 [10 refs]

Working with suspensions of sporozoites of *Plasmodium gallinaceum* in a mixture of equal parts of chick serum and physiological saline and with suspensions of infected red blood corpuscles in citrate-saline solution the authors have tested the effect on the infectivity of such suspensions of exposure to X ray irradiation of varying intensity. The sporozoites were inactivated by 8 000 roentgens as proved by failure to produce infection on intramuscular injection. In the case of the trophozoites the suspension which was of such a strength that 0.1 cc. contained 16 000 000 parasitized red blood corpuscles was inactivated by 20 000 roentgens as proved by intravenous inoculation of 0.1 cc amounts. Less than 10 000 roentgens altered the parasites in such a manner that after inoculation the prepatent periods and survival times were increased. Attempts to increase the survival time of infected chicks by exposing them to radiation were not successful. In one experiment it was shown that the exposure of human blood infected with *P. malariae* to 5 000 roentgens rendered it non infective as proved by injection into a patient with central nervous system syphilis.

C M Wenyon

COVELL G. Notes on the Distribution Breeding Places, Adult Habits and Relation to Malaria of the Anopheline Mosquitoes of India and the Far East *J Malaria Inst of India* 1944 Dec. v 5 No 4 399-431 1 folding map [Numerous refs.]

The title of this paper describes its scope. Only those species of anopheline mosquitoes are dealt with which either have been found naturally infected with malaria or have been suspected on epidemiological grounds to transmit the disease. The area surveyed includes India countries of the continent of Asia south of and including South China and the islands from Formosa in the north to Australia in the south from the Andamans and Nicobars in the west to the New Hebrides and New Caledonia in the east. More than 100 species of *Anopheles* have been described from these regions of which only 41 have been proved or suspected to be vectors of malaria only these 41 species are referred to. Two groups of species have been of great importance during the war—the *fluvialis minimus* group which is responsible for intense malaria in the foothills of north India and in Burma and South China and *A. punctulatus* with its variety *moluccensis* which are responsible for intense malaria in New Guinea and the S W Pacific Islands.

There are 12 important malaria vectors *A. culicifacies* *A. fluvialis* *A. maculatus* *A. minimus* *A. minimus* var *flavirostris* *A. philippinensis* *A. punctulatus* *A. punctulatus* var *moluccensis* *A. stephensi* *A. sundanicus* *A. superpictus* *A. umbrosus*.

Sixteen species are of local importance as vectors in certain areas. These are *A. aconitus* *A. annularis* *A. bancrofti* *A. barbirostris* *A. hyrcanus* var *nigerrimus* *A. hyrcanus* var *sincensis* *A. hyrcanus* \ *A. geyroporiensis* var *candidiensis* *A. kochi* *A. leucosphyrus* *A. novumbrus* *A. pattoni* *A. stephensi* var *mysorensis* *A. subpictus* var *indefinitus* *A. tessellatus* *A. varuna*.

the results thus on the infectivity of *Anopheles culicifacies* Giles. *J Malaria Inst of India* 1944 June v 5 No 3 375-88 [27 refs.]

one but then account of observations made in Calcutta on the influence of temperature and humidity on the infectivity of *A. culicifacies*. Biological incubators and an air-conditioned cool room were used. *A. culicifacies* were bred from full-grown larvae or pupae collected in the wild. Attempts at colonizing this species were unsuccessful.

Lowering of the temperature within the range 94° to 70°F increases the period of survival of *A. culicifacies* especially if the decrease be combined with increased relative humidity. Mean temperatures below 60°F and humidities below 60 per cent are inimical to this species. Indian strains of *P. vivax* and *P. falciparum* do not develop in *A. culicifacies* at temperatures above 94°F. The optimum range of temperature for development in the mosquito and for transmission is from 70° to 86°F provided humidity is sufficient for the survival of *A. culicifacies*. The lower limiting temperatures for the development of parasites in this species were not determined. Oöcyts of *P. falciparum* and of *P. vivax* have been found at a mean temperature of 59.6°F but *P. malariae* did not develop at all in these conditions. The extrinsic incubation period of the parasites varied from seven days for *P. vivax* at 86°F and 19 days for *P. malariae* at 70°F.

Norman White

VISWANATHAN D K, RAO T R & RAO T S R. The Behaviour of *Anopheles fluviatilis*. Part II. Nocturnal Movements and Daytime Resting Places and their bearing on Spray-Killing. *J Malaria Inst of India* 1944 Dec v 5 No 4 449-61

An examination of mosquitoes captured in dwelling houses in the North Kanara District in the extreme south of the Bombay Presidency indicated that about 60 per cent of female *A. fluviatilis* leave the house for some outside resting place every night during the months of September to November when the gonotrophic cycle [the period during which a blood meal is digested and the eggs mature] takes 48 hours in the laboratory. From December to February 40 per cent. behave in this fashion. The duration of the gonotrophic cycle is then 72 hours. Direct experiment confirmed this finding. Most freshly fed *A. fluviatilis* left their places of feeding between the time of feeding and dawn. These observations have an obvious bearing on the use and limitation of spray killing as a malaria control measure where this species is the vector. The authors recommend that in sparsely populated areas in North Kanara daily spraying should be used. In larger centres of population where some larval control is possible spray-killing twice a week is recommended during that part of the transmission season when the duration of the gonotrophic cycle is 72 hours. When the duration of the cycle is 48 hours spraying should be carried out on two consecutive days with intervals of two days without spraying.

Some 71 per cent of *A. fluviatilis* which enter dwellings do so during the first quarter of the dark hours 19 per cent during the second quarter 7 per cent in the third quarter and 3 per cent in the last quarter.

Norman White

IVENGAR M O T. Problems relating to Malaria Control in Deltaic Bengal. *J Malaria Inst of India* 1944 Dec v 5 No 4 435-47

A. philippinensis is the only important vector of malaria in the deltaic region of Bengal excluding the estuarine zone. There is a significant positive correlation between the prevalence of this species and malaria endemicity. No other species except for occasional single observations has been found naturally

infected. *A. philippinensis* is relatively infrequent during the first half of the year and sporozoite infections are then rare. The period of maximum transmission is from September to November.

Human dwellings are the favoured daytime resting places of *A. philippinensis*; it is infrequently found in cattle-sheds. It generally rests on the wall very close to the floor. The main breeding season of this species is the rainy season, July to October. Ponds with clean water free from organic pollution are the favoured breeding places. Submerged aquatic vegetation reaching the surface as subaquatic bushes favours breeding, whilst any shade-producing plant is inhibitory. A dense growth of the water hyacinth *Eichornia speciosa* effectively controls the breeding of *A. philippinensis*. Areas in Deltaic Bengal with a high water table have a low prevalence of *A. philippinensis*; drainage as an anti-malaria measure is therefore contraindicated and wet cultivation should be encouraged. This species does not ordinarily breed in ricefields.

The control of *A. philippinensis* should include the insecticidal spraying of dwelling rooms, the control of breeding in ponds by complete removal of all forms of aquatic vegetation or by stocking them with water hyacinth so as to form a complete cover, raising the water table by irrigation or other method.

Norman White

HESS A D & HALL, T F. The Relation of Plants to Malaria Control on Impounded Waters with a suggested Classification. *J. National Malaria Soc. Tallahassee Fla.* 1945 Mar v 4 No 1 20-48 2 figs. [23 refs.]

Anopheles quadrimaculatus, the only important malaria vector in the South-eastern United States, breeds solely in waters on which there is an abundance of vegetation or floatage intersecting the water surface. "a clean water surface does not produce quads." This fact explains the extensive work that has been carried out by the Health Department of the Tennessee Valley Authority on the relation of plants to malaria control on impounded waters [see this *Bulletin* 1945 v 42 182].

This paper contains a classification of plants in relation to malaria control. All plants of importance to malaria control in the Tennessee Valley are placed in ten basic types, each having well-defined relationships to the biology and control of *A. quadrimaculatus* in impounded waters. The large mass of information does not lend itself to adequate summary in small space. Though the results of the painstaking investigations are of local rather than general interest and importance the methods employed will interest a large number of malariologists in distant fields who have cognate problems to solve. They should consult the original paper.

Norman White

SCHOOF H F, SCHELL S C & ASHTON D F. Survival of Anopheline Larvae and Pupae in Mud. *J. Econom. Entom.* 1945 Feb v 38 No. 1 113-14.

In N. Carolina, on several occasions, high adult anopheline counts could not adequately be explained by the data on collections of larvae. It occurred to the authors that larvae and pupae may be able to persist in mud, and that if so they might live in certain creeks which were from time to time filled by wind tides which are not subject to regular periodicity. Mud was therefore placed in a bucket and water added. Larvae and pupae (*Anopheles quadrimaculatus* and *A. punctipennis*) was placed in the water which was then carefully removed until the surface was reduced to the consistency of thick mud. After 29 hours in this mud most of the larvae and all the 4 pupae were alive; after 48 hours only a few of the larvae survived, but 4 of 4 pupae were still alive. From some of these adults developed.

Examination of a dry ditch with a slimy bottom, into which waste water from a house was run showed that 3rd and 4th stage larvae and some culicine pupae appeared they must have been present in the mud but for how long is not stated.

This work evidently needs to be amplified and the fact that larvae and pupae can survive for some time in mud [the authors use the rollicking word much] must have a bearing on anti larval methods of anopheline control

Charles Wilcocks

BARNES R. C. *Anopheles walkeri* in Diurnal Shelters in Massachusetts. *J Econom Entom*, 1945 Feb v 38 No 1 114

EYLES D. E. & BURGESS R. W. *Anopheles walkeri* in South Carolina. *J Econom Entom* 1945 Feb v 38 No. 1 115

McCLURE R. D. & LAM C. R. Malaria from Bank Blood Transfusions. *Surgery Gynecol & Obstet* 1945 Mar v 80 No 3 281-2.

Comparatively few instances of the transmission of malaria by blood transfusion have been reported. WRIGHT (*J Pediatr* S. Louis 1938 v 12 327) collected 23 cases from the literature and added six of his own. GORDON [this *Bulletin* 1942 v 39 252] described the first recorded case of transmission by stored blood and added five more references (McCULLOCH *Canadian Med Ass J* 1937 v 37 26. GARDNER and DEXTER this *Bulletin* 1939 v 36 783. ZUSSMAN and SILVER *Med Rec* 1938 v 148 176. NABARRO and EDWARD this *Bulletin* 1940 v 37 362 and CHANORRO and MOLEZZUN *Semana Med* 1938 v 2 908) [For other records see this *Bulletin* 1940 v 37 456 1941 v 38 505 1944 v 41 8 and 92 and 1945 v 42 174.]

In the present paper the authors report two cases of transmission with blood which had been refrigerated for five days. In each case the donor was an Italian man born in Sicily who had lived for over 30 years in the United States of America. These two donors were uncles of a youth whose blood bank debt they were paying by becoming blood donors. In both cases quartan malaria parasites were transmitted.

The first patient a woman of 57 years was given 600 cc. of citrated blood during an operation. Her temperature rose to 101°F on the following day, remained normal until the 32nd day when it rose to 101°F and rose again on the 35th day to 100.6°F but no chills were recorded. She was discharged from hospital but was readmitted two weeks afterwards complaining of having had attacks of nausea and vomiting preceded by rigors. On admission her blood showed erythrocytes 3 100 000 per cmm. leucocytes 2,350 per cmm. with 67 per cent of polymorphonuclears. Examination by X rays indicated splenic enlargement but this was ignored. On the following day her temperature rose to 105°F and next day quartan malaria parasites were found in her blood. Treatment with quinine was effective.

The second patient a woman aged 23 received 500 cc. of citrated blood during an operation and remained afebrile from the 3rd to the 22nd day when she was given another blood transfusion—this time with the blood of a professional donor who had never been in a malarious country and had often given blood without mishap. Her temperature rose at once to 101.6°F but was normal next day and she was discharged on the 23rd day after the operation with instructions to record her temperature. Three days later her temperature was 102.6°F and a fortnight after this she reported that chills and fever occurred every third day blood smears were negative. Her temperature remained

of the psychoses is a possibility. There was no evidence that the patients who developed post malaria-mepacrine psychoses were psychiatrically unstable [except of course, as a result of taking mepacrine] Norman White

RUSSELL H K Eosinophilia caused by Atabrine. *U.S. Nav Med Bull* 1945 Mar v 44 No 3 574-5

A study was made of the eosinophil count in men taking mepacrine (atabrine) in the tropics. A careful examination of the stools was made to detect hookworm ova, and only men who were free from them were accepted. Of 119 patients on mepacrine therapy for malaria and who had been in the tropics for an average period of 14 months 80 (75 per cent) showed an eosinophilia of 6 per cent or over the highest was 27 per cent. The average for the 119 men was 8.4 per cent. Among 50 men on suppressive mepacrine whose skin was stained yellow by the drug and who had been in the tropics for an average period of 10 months 36 (70 per cent) showed an eosinophilia of 6 per cent or more the maximum was 22 per cent. The average for the whole group was 7.2 per cent. Among 33 men who had never taken mepacrine and who had been in the tropics for an average period of eight months two had eosinophil counts of 6 and 7 per cent respectively. The average for the whole group was 3 per cent. Bone marrow aspiration biopsies in 16 cases showed marked hyperplasia of the eosinophilic cells. It is believed that this is due to the mepacrine F. Hawking

JANG C S Present Status of Studies on Chinese Antimalarial Drugs. *Chinese Med J* Washington D C 1944 Apr-June v 62 No 2 185-92.

"Scientific studies on the Chinese antimalarial herbs have been surveyed. While the antimalarial value of *Simine* (from *Fraxinus mollicophyla*) requires further investigation the clinical experiments with *Anobin* (probably from *Euphorbia salacensis*) and *Fraxin* (from *Fraxinus chinensis*) have not been able to demonstrate any antimalarial effect. *Chang Shan* (*Dickroa febrifuga*) appears to be most promising as an antimalarial remedy the clinical results being quite comparable with those of quinine. Two alkaloids have been isolated from *Chang Shan* and their chemotherapeutic studies are in progress.

FAIRLEY N H Chemotherapeutic Suppression and Prophylaxis in Malaria. An Experimental Investigation undertaken by Medical Research Teams in Australia. *Trans Roy Soc Trop Med & Hyg* 1945 May v 38 No 5 311-35 4 graphs Discussion 355-63 (JAMES S. P. SHUTE P. G. HODGE E. H. V. MACDONALD G. REID J. FINLAY G. M. MACGRAITH B. SINTON J. A. ROGERS, L. and FAIRLEY N. H. (in reply))

The high incidence and gravity of malaria among troops in the South-Western Pacific Area prompted the establishment of two research groups in tropical Queensland, under the direction of the author to investigate the mode of action and the precise value of anti-malarial drugs—including certain new sulphonamides mepacrine and quinine—as suppressants and true causal prophylactics in volunteers infected with Papuan strains of both *P. vivax* and *P. falciparum*. Volunteers taking anti-malarial drugs in a specified daily dosage were exposed to bites of malaria-infected mosquitoes, and were studied throughout the incubation period of malaria. They were then sent inland to another Australian General Hospital where the second group of research workers continued investigations to determine whether the drug in question had merely suppressed the infection or cured the patient.

For this experimental transmission of malaria *A. punctulatus* var *typicus* was mainly used. It survived better under laboratory conditions and was a more efficient all round transmitter than either *A. punctulatus* var *moluccensis* or *A. annulipes* it had a high average infection rate. The larvae were collected in New Guinea and flown to Queensland some 20 000 a week.

Volunteers were restricted to men who had never lived in malarious areas and who were organically sound physically fit and mentally stable. The experiments were carried out on a very large scale but no evidence of insusceptibility or natural immunity to these New Guinea strains of *P. vivax* and *P. falciparum* was ever demonstrated. It would seem that no European who has not previously been exposed to malaria is ever refractory to infection if viable sporozoites or trophozoites of *P. vivax* or *P. falciparum* be inoculated in a reasonable dosage.

It is not possible to give an adequate summary of the large mass of information contained in this important contribution. The main conclusions are —

Quinine sulphate given in solution 10 grains daily commencing two days before the first infective bite failed to prevent overt attacks of *falciparum* malaria. Similar doses completely suppressed *vivax* attacks in some cases but not in all.

Certain sulphonamides (sulphadiazine sulphamerazine and sulphamerazine) in doses of 1.0 gm daily suppressed *falciparum* malaria in 20 out of 21 volunteers and cured 17 of the 21. These drugs are not causal prophylactics they destroy the asexual blood parasites. They failed to suppress *vivax* infections. 21 of 24 volunteers had clinical attacks while taking 1.0 gm a day. The remaining three developed attacks shortly after the end of treatment.

Mepacrine 0.1 gm daily suppresses *falciparum* malaria and if continued for the requisite period after the last exposure to infection cures the disease. In these experiments the drug was continued for 23 days after the last bite when exposure to infective bites did not exceed seven days. Subinoculation tests proved the action of mepacrine to be on the asexual blood parasites. Mepacrine in these doses also suppresses *vivax* malaria but clinical attacks regularly occur a few weeks after the cessation of treatment. Hard physical work and exposure of the subjects to arduous conditions comparable to those experienced on active service, did not rob mepacrine of its efficacy.

The experiments have shown that a correct mepacrine regimen may secure the control of malaria in hyperendemic areas. This knowledge has been applied with dramatic results. In December 1943 the malaria rate in Australian troops in New Guinea was 740 per 1 000 per annum. In November 1944 this rate had fallen to 28. Other causes have been at work there was less fighting in 1944 and antimosquito measures were more effective but the absence of frequent *vivax* relapses indicated a high standard of mepacrine discipline.

The problem of *vivax* relapses after the cessation of mepacrine treatment remains. Malaria due to the New Guinea strain of *P. vivax* is characterized by the following features: (1) relapses appear within a few weeks of the primary fever or cessation of treatment. (2) though febrile attacks are readily controlled by drugs the subsequent relapse rate is very high. The experiments indicate that the tissue forms of *P. vivax* are very persistent whereas the tissue cycle of *P. falciparum* seems to be of short duration.

Subinoculations by direct blood transfusions of not less than 200 cc. of blood were frequently used to determine the infectivity of blood. Seven minutes after biting has ceased on one arm blood from the other arm has produced malaria in the recipient in both *falciparum* and *vivax* infections showing that sporozoites were circulating. No such positive results were obtained 30 minutes after biting the sporozoites are rapidly removed by macrophages and fixed tissue endothelial cells. Thereafter for several days negative results only were obtained. In *P. falciparum* infections subinoculations from the seventh day

onwards but not before transmitted malaria in *P. vivax* infections sub-inoculations were invariably negative till the ninth day thereafter positive results were obtained
Norman White

MINGOJA, Q. Medicamentos quimioterápicos antimaláricos. [Anti Malarial Drugs.] *Seleção Chimica* São Paulo. 1944 Dec. No. 1 5-120 7 figs. [Numerous refs.]

This is a review of the literature on the subject. It deals with quinine and other cinchona derivatives, plasmoquine and other substances of the quinoline series, mepracrine and with other synthetic preparations. There is a good deal of chemical information, and the structural formulae of a large number of drugs are presented. This article will be very useful as a work of reference for those who read Portuguese.
Charles Wilcocks

RICE, P. L., HUFFAKER, C. B. & BACK, R. C. DDT Thanite Sprays for Mosquitoes. *Soap* New York, 1945 Mar. v 21 No 3 119 121 & 146 2 figs.

Investigations which were started as a result of the shortage of pyrethrins have led to the development of sprays containing a mixture of 2,2-bis (parachlorophenyl) 1,1,1-trichloroethane (DDT) and Thanite (a terpene thioacyano ester). In laboratory tests the standard Peet-Grady testing chamber was employed with six ml. of insecticide and a two and a half minute exposure. The test insect was *Anopheles quadrimaculatus*. Field tests were also carried out in a cattle shed, open on one side. The insecticide was sprayed about three to four feet away from the wall on which the cages were suspended, 6.5 ml. of spray being discharged over 48 sq. ft. of surface.

In the Peet-Grady test it was found that a 1 per cent. solution of DDT gave a 57 per cent. knock-down after two and a half minutes and a 100 per cent. kill 24 hours later. With a solution containing 0.2 per cent. DDT and 0.80 per cent. Thanite the knock-down was 92 per cent. and the kill 96 per cent., while 0.4 per cent. DDT and 0.6 per cent. Thanite gave 86 per cent. knock-down and 99 per cent. kill. In comparison a spray of 0.02 per cent. pyrethrins gave a knock-down of 97 per cent. and a kill of 94 per cent. The advantage of adding "Thanite" is that it increases the rate of knock-down, but the DDT is mainly responsible for the lethal action of the spray.

In the field tests the authors used one and one-half times the concentration of toxic ingredients employed in the laboratory tests, and the mixed sprays again gave satisfactory knock-downs and kills. A spray of pyrethrins also of one and a half times the concentration used in the Peet-Grady test gave approximately the same knock-down as the mixed sprays while the 24 hour percentage kill was about 20 per cent. less.
W. A. L. David

KANCHAVELI, G. I. [Employment of Emulsions of Mineral Oils for the Control of Anopheles Larvae.] *Med. Parazit. & Parasitic Dis.* Moscow 1944 v 13 No 4 83-5 [In Russian.]

An account is given of the larvicidal effect of various mineral substances tested as substitutes for Paris green and petroleum, the use of which had to be restricted owing to war conditions. Promising results were obtained with kerosene green oil and a preparation known as "flycide". These were emulsified with delphinium (or green) soap in the following proportions: 1 part soap + 0.5

water+5 to 10 parts larvicide. The mixture was sprayed over natural water collections in which *Anopheles* larvae were present in doses of 0.3-0.5 gm. per 1 sq metre of the surface the higher dose thus containing 0.04 gm. of soap and 0.43 gm of larvicide. This treatment resulted in the destruction of 100 per cent. of the larvae starting 2-3 hours after application, the oily film of the larvicide remaining on the surface of the water up to 72 hours at 19.5-27.5°C. These emulsions have no harmful effect upon the remaining fauna and flora of the water their only drawback being the rapid evaporation of the larvicide.

C A Hoare

MULRENNAN J A GOODWIN M & SHANNON R. C The Importation of Exotic Anophelines Into the United States J National Malaria Soc Tallahassee Fla. 1945 Mar v 4 No 1 56-8.

In August 1943 a dead *Anopheles* (*Nyssorhynchus*) in a spider web was found under a concrete bridge a mile from the runway on the Morrison Field air base West Palm Beach. In May 1944 a single fourth instar *A. albimanus* larva was found in a canal running through the Boca Raton Army Air Field. There was presumptive evidence that a female *A. albimanus* came in by plane from Porto Rico and oviposited at Boca Raton. These are the first records of *A. albimanus* having been collected in Florida since 1904 when it was imported into Key West from Vera Cruz. During the first nine months of 1944 38 anophelines all dead were collected during quarantine inspections of airplanes at Miami Florida. They included *A. crucians*, *A. grabhami*, *A. walkeri*, *A. albimanus*, *A. pharoensis* and *A. (Nyssorhynchus)* species. It would appear that without constant vigilance foreign species of anophelines might enter and become established in the United States. It is important that aircraft should be effectively treated with insecticide at the port of departure and the process repeated at the port of entry.

Norman White

See also below p 656 FAIRLEY Medicine in Jungle Warfare

CANTRELL W & JORDAN Helen B New Mosquito Hosts for *Plasmodium gallinaceum* J Parasitology 1945 Feb v 31 No 1 55-6

Nine species of mosquito wild or laboratory bred were allowed to feed on chickens infected with *Plasmodium gallinaceum* and were dissected from 3 to 9 days later and examined for the presence of oöcysts a few were examined for sporozoites and oöcysts after 9 to 21 days. Seven of the species had not previously been studied in this respect they were *Aedes campestris*, *A. stimulans*, *A. biserratus*, *A. trivittatus*, *Culex salinarius*, *Mansonia perturbans* and *Theobaldia inornata*.

Oöcysts were found in all the species in varying numbers but this variation was not necessarily related to susceptibility as different chickens were used in the experiment.

All species of *Aedes* so far tested have been found susceptible.

No infection was found among 120 *Culex pipiens* which were also fed, thus confirming BRUMPT's conclusion (Ann Parasit. Hum et Comp. 1936 v 14 597) that this species is resistant.

J F Corson

BLACKWATER FEVER.

FOY H. HOWE, Athena, RUBENLO A. & SOEIRO A. Survival of Transfused Red Cells in Blackwater Fever Circulation and of Blackwater Red Cells in Normal Circulation. (Preliminary Report) *Trans Roy Soc Trop Med & Hyg* 1945 Mar v 36, No 4 271-86 3 charts. [19 refs.]

The authors transfused blood group A cases of blackwater fever with compatible group O blood, and a normal healthy person with blood cells from a group O case of blackwater fever. The survival time of the transfused cells was estimated by the method of differential agglutination (*ASHBY J Exper Med* 1919 v 29 267).

They also transfused serum from a blackwater fever case into a patient suffering from an acute attack of subtertian malaria.

Making due allowance for the limitations of the methods used and the restricted material available the authors obtained the following results—

(1) Transfused cells are destroyed in blackwater fever haemolysis as readily as the patient's own cells.

(2) The survival time of normal red cells transfused into cases of blackwater fever nine days after haemolysis had stopped was 30-35 days after 18 months the survival time was normal.

(3) Cells taken from a haemolyzing blackwater fever case and transfused into a normal group A recipient had a survival time of only six days.

A single experiment in which cells from a blackwater fever group O patient were taken in a quiescent period 10 days after haemolysis and injected into a normal A group recipient was inconclusive as the donor developed further haemoglobinuria five days after the blood had been withdrawn. The survival time of these cells was shorter than normal.

(4) Plasma from a blackwater fever case laden with oxyhaemoglobin and methaemoglobin transfused into a patient with acute malaria had no haemolytic effect.

This paper is interesting and stimulating. There is a brief discussion of the various theories of the nature of haemolysis in blackwater fever and haemolysis in this disease is compared with that in haemolytic jaundice (*DACE and MOLLISON Lancet* 1943 May 1 550).

The authors conclude from their results that in blackwater fever at least, the fundamental factor is extra-cellular and can haemolyze normal cells in the blackwater fever circulation, as well as bring about changes in the blackwater fever red cells that render them susceptible to destruction even in normal circulations. Thus the situation in haemolytic jaundice and blackwater fever would appear to differ in that whatever brings about the lysis of the red cells in haemolytic jaundice is not capable of affecting normal red cells transfused into patients with active haemolytic jaundice."

[The discussion would have been more effective if the authors had had access to the work of BROWN *et al* (*Bulletin of War Medicine* 1944 Dec v 5 No. 4 250) who investigated the fate of transfused cells in a wide variety of anaemic conditions and to that of POWDER (*J Gen Phys.* 1944 v 27 283) regarding haemolysis by normal tissue.]

B G Macgregor

LEISHMANIASIS

BURCHENAL J H & WOODS R P Visceral Leishmaniasis Report of Three Cases of its Occurrence in Members of the Armed Forces of the United States *War Medicine* Chicago 1945 Mar v 7 No 3 173-7 1 chart

The paper describes three cases of leishmaniasis in men of the U.S. Army who had served in N. Africa and Sicily. Two of these were typical cases of kala-azar in each of which there was some difficulty in discovering leishmania. However, in both parasites were eventually found, in the first case at the third sternal puncture and in the second at spleen puncture after two unsuccessful sternal punctures. In both cases treatment with diamidmostilbene was tried without success, reliance being finally placed on sodium antimony gluconate. In various courses the first patient had 282 cc. intravenously (representing 5.640 mgm. of antimony) and the second 252 cc. representing 5.040 mgm. of antimony. It is of interest to note that during the antimony therapy both patients suffered relapses of benign tertian malaria, which had to be controlled by quinaquine [mepacrine] hydrochloride.

The third case is of particular interest in that the only symptom complained of by the patient was a visible swelling of the post-cervical and post-auricular lymph nodes. Physical examination revealed essentially a normal condition except for enlarged suboccipital, post-auricular and posterior cervical nodes. The largest measured 1.5 by 2.0 cm. The epitrochlear nodes were just palpable and a few discrete axillary nodes were felt. The only other possible sign was a slight tenderness of the liver which descended 2 cm. below the costal margin on deep inspiration. As all laboratory examinations including sternal puncture failed to assist in a diagnosis a lymph node was excised. In sections stained by Giemsa stain leishmania were identified. Attempts were made to confirm this finding by examining smears of fluid aspirated from other enlarged lymph nodes. This was unsuccessful. Finally a second node was excised and in smears of this leishmania were again found. As a diagnosis of leishmaniasis was now firmly established a course of injections of solution of sodium antimony gluconate (90 cc.) was given in spite of the patient's apparent excellent health.

The paper gives no account of the subsequent history of these cases.

C. M. Wenyon

FEVERS OF THE TYPHUS GROUP

WERTMAN K. Nonspecific Complement-Fixing Antigen in Embryonic Egg Tissues *J. Lab. & Clin. Med.* 1945 Feb v 30 No 2 112-18. [15 refs.]

The author has found that when relatively crude egg yolk cultures of rickettsiae are used as antigens in the complement fixation tests for fevers of the typhus group, an appreciable amount of non-specific antigen derived from the egg yolk is retained in the suspension. With the specially sensitive technique consisting in primary incubation for 18 hours at 4-8°C. the non-specific antigen may give rise to a false-positive reaction. With the less sensitive technique of incubation at 37.5°C. for one hour the titre of the reactions is considerably lower. The non-specific antigen is of the Wassermann type and so with the sensitive technique reactions would occur with Wassermann positive sera.

By repeated washing and centrifugation the non-specific antigen is removed at the Army Medical School, Washington. Plotz (this *Bulletin* 1943 v 40 443) uses a highly purified antigen prepared in this way.

BENGTSON (this *Bulletin* 1941 v 33 682 and 690), in her experiments used antigen purified by only one centrifugation but as she adopted the less sensitive technique no false positives would have been likely to occur.

John W. D. Megaw

Plotz, H. BENNETT B., WERTMAN K. & SNYDER, M. Cross-Reacting Typhus Antibodies in Rocky Mountain Spotted Fever. *Proc. Soc. Exper. Biol. & Med.* 1944 Dec., v 57 No 3 336-9

In this important paper the authors throw a flood of light on the immunological relationship between Rocky Mountain spotted fever epidemic typhus and murine typhus.

The following table has been extracted from the fuller one contained in the article. It shows the types of responses to various tests given by sera of persons infected with Rocky Mountain spotted fever (R.M.S.F.).

The tests were —(1) Weil-Felix tests in which *Proteus* OX19 and Pr OX2 were used. (2) Complement fixation tests for R.M.S.F. epidemic typhus (E.T.) and murine typhus (M.T.). (3) Rickettsia-agglutination tests in which epidemic typhus rickettsiae (E.T.R.) and murine typhus rickettsiae (M.T.R.) were used, and (4) Mouse-neutralizing tests showing the richness of the patients' sera in antibodies capable of neutralizing epidemic typhus toxins derived from yolk sac cultures (M.N.T. ep. typhus).

Titres in Tests of Sera from Cases of Rocky Mountain Spotted Fever

Day of disease	Weil-Felix		Complement Fixation			Rickettsial agglutination		M.N.T. ep. typhus
	OX19	OX2	R.M.S.F.	E.T.	M.T.	E.T.	M.T.	
(1) 14	640	0	160	0	0	640	640	6,510
15	640	0	160	0	0	80	2,560	1,444
(2) 16	0	0	20	0	0	—0	—0	2,888
(3) 18	2,560	160	40	0	0	—	—	64
(4) 6	0	0	0	0	0	0	80	—
49	320	40	40	0	0	0	160	6
(5) 40	320	320	180	0	0	0	80	45
(6) 130	40	80	80	0	0	0	80	128
(7) 12	640	0	80	0	0	80	160	—
(8) 44	0	180	640	0	0	0	80	—
(9) 29	160	2,560	80	0	0	0	40	—

The Weil-Felix responses were of the irregular type usually observed in tick borne typhus. Neither this nor the rickettsia-agglutination reaction appears to afford a means of differentiating tick borne from louse-borne and flea borne typhus. The complement-fixation test has given uniformly consistent results in this respect.

Further evidence regarding the mouse neutralizing test is given in two other tables from which the following figures have been taken to illustrate the results obtained with sera from persons who had suffered from epidemic typhus and Rocky Mountain spotted fever.

Titres observed in Mouse neutralizing Tests (Epidemic Typhus)

Sera from Epidemic Typhus Cases		Sera from R.M.S.F. cases	
Day of Disease	Titres	Day of Disease	Titres
99		57	204
104	256	106	23
117	814	120	132
137	102	130	128
218	180	217	8
	40		

These figures show that antibodies capable of neutralizing the toxins of epidemic typhus are present in considerable amounts in persons who have recovered from Rocky Mountain spotted fever so that this test also cannot be relied on for differentiating the two diseases either in the active stage or after recovery

John W D Megaw

DAMON S R. & JOHNSON Mary B The Serologic Diagnosis of Endemic Typhus I. The Use of specially prepared Rickettsial Suspensions and Commercial Typhus Vaccines as Antigens in the Complement Fixation Test. *J Lab & Clin Med* 1945 Mar \ 30 No 3 233-6

The purpose of this study was to compare the relative values of specially prepared rickettsial suspensions and commercial typhus vaccines as antigens in complement fixation tests for endemic (flea borne) typhus. Four of the special suspensions were prepared from strains of endemic rickettsiae and one from an epidemic strain. All the commercial vaccines were of the epidemic type. The sera used in the tests were from (a) guinea pigs that had recovered from endemic typhus or (b) from active cases of endemic typhus in human patients.

With water bath fixation for one hour the endemic rickettsial antigen when freshly made could be used in dilutions of 1-16 to 1-32 that is using 4 units in the test the unit being the smallest amount which gave complete fixation with the standard serum. There was some loss of antigenicity in stored suspensions but they were still useful for 4-8 months. The special suspension of epidemic rickettsiae had to be employed in dilutions of 1-1 or 1-2.

Commercial epidemic typhus vaccines made by Parke Davis and the Lederle Laboratories were found suitable at dilutions ranging from 1-2 to 1-4 and they had good keeping properties. Vaccines made by Eli Lilly and Co were entirely unsuitable.

The authors suggest that the higher antigenic titres obtained with the special suspensions may be accounted for by their greater concentration or by their being prepared from endemic rickettsiae.

[The latter explanation would seem to be the more reasonable two of the commercial vaccines compared favourably with the special suspensions made from epidemic rickettsiae and a higher titre reaction would be expected to occur with a homologous than with a heterologous rickettsial antigen. The failure of the Eli Lilly vaccine proves only that it does not contain antigens of the heterologous type. It might possibly be rich in antigen of the strictly epidemic type if so it would be an effective vaccine against louse-borne typhus and also an ideal source of antigen for differentiating that disease from flea borne typhus.

This paper should be read in conjunction with the preceding articles by WERTMAN and by Plotz and his collaborators.]

John W D Megaw

HALLERVORDEM J. Die pathologisch-anatomischen Veränderungen im Zentralnervensystem beim Fleckfieber [The Pathological Anatomy of the Central Nervous System in Typhus Fever] *Deut. Militärarz.* 1943 Jan., v 8 No. 1 28-30 5 figs.

A detailed account is given of the naked-eye and microscopical changes found in the central nervous system in typhus fever. The paper is illustrated by five good reproductions of photomicrographs showing the 'typhus nodules' at various magnifications.

Although the nodules are specially associated with the arterioles and capillaries they are not infrequently found in the adjacent tissues near to but apart from, the vessels. The author states that by histological examination alone it is not possible to differentiate the cerebral lesions of typhus fever from those occurring in various forms of encephalitis of quite different aetiology.

Many references are made to the findings of other observers.

John W. D. Megaw

SKOKIN I. E. & KORSHUNOVA O. S. [Chemotherapy of Typhus exanthematicus (Preliminary Communication)] *Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii* Moscow 1944 No 10-11 77-82. [In Russian.]

Mice were inoculated intranasally with rickettial suspension, and various compounds were given by mouth at the same time and also twice on the following day. Guinea-pigs were also used in some tests. The chemotherapeutic activity of a compound was assessed by its ability to prolong the survival period of test animals as compared with untreated controls. In all, 56 compounds were tested. Some activity was found in 8 of 13 N^1-N^4 disubstituted sulphanil amides: sulphaguanidine lengthened survival time 2.5 times and 2 of 6 mice survived. Three of 7 diphenylsulphide-sulphonide-sulphones tested also had some effect (survival time lengthened $\times 1.7$). The remaining compounds (including N^1 and N^4 substituted sulphanilamides, azo-substituted compounds, sulphanilamide substituted in the nucleus, organo-metallic derivatives of sulphanilamide and others) were all inactive.

D. J. Bauer

PESTANA, B. R. Considerações epidemiológicas a respeito do tifo exantemático em São Paulo [Epidemiological Studies in the Exanthematic Typhus of São Paulo.] Reprinted from *Anais Paulist. de Med. e Cirurgia* São Paulo 1944 Oct v 48 No 4 227-347 5 figs. [63 refs.] English summary.

The author discusses at considerable length the epidemiology of this fever which is generally accepted as being ~~immunologically~~ the same as Rocky Mountain spotted fever. While admitting that two types of typhus fever may occur in the region, he argues that there is much to be said for the view that the disease is murine typhus transmitted by fleas.

The plea for further investigation of the probable vectors, reservoirs of infection, and causal rickettsiae can be heartily supported, because São Paulo obviously is a rich field for study of the typhus fevers.

The author states that in all the 75 patients who recovered at the isolation hospital, the Weil-Felix reaction was positive with *Proteus* OX19 at titres of 1-1 000 to 1-30 000 whereas in the 204 who died the reaction was negative or positive at relatively low titres only. The reaction with *Pr* OXA was usually negative, but in some patients it was positive at titres ranging up to 1-1 600.

In view of the very high fatality rate and the convincing evidence provided by PARKER and DAVIS and other workers that the disease is closely related to

if not identical with Rocky Mountain spotted fever it seems likely that this is the predominant type of infection but the coexistence of flea borne typhus would not be surprising

John W D Megaw

KIBLER M Vom Funftagefieber und seiner Bedeutung für die Differentialdiagnose [The Differential Diagnosis of Five-Day Fever [Trench Fever] and Its Importance.] *Deut Militärarz* 1943 Feb v 8 No 2 100-104

The author states that most of the textbooks deal chiefly with the differential diagnosis of trench fever with special reference to malaria, undulant fever and relapsing fever in his own experience difficulty arose most frequently in connexion with influenza, paratyphoid B typhus fever and wound sepsis. Special stress is laid on the great variability of the clinical features of the disease not only in different epidemics but also in the course of the same epidemic.

In the early stages it may be very difficult to exclude influenza but in trench fever there is often a painful enlargement of the spleen a localization of the pains in the thighs and shin bones, and diarrhoea. The more sudden rise of the temperature the absence of mental symptoms and of the characteristic facial expression observed in typhus fever help to exclude this disease. Although the incubation period in trench fever is usually less than 14 days it may be as long as 60 days. The blood may be infective for long periods so that it is not safe to employ a patient as a blood donor till two years have elapsed. The periodicity is usually of the five-day type but it may range from the two-day to the seven-day type even in the course of the same attack.

John W D Megaw

BADER M. & ANIGSTEIN L. Specificity of Bullis Fever Rickettsia. *Texas Reports on Biol & Med* 1944 v 2, No 4 405-12.

The authors describe the results of further investigations into the strains of infection whose isolation they have already reported [see this *Bulletin* 1944 v 41 666]

The strain of rickettsia isolated from *Amblyomma americanum* at Camp Bullis in 1943 [this *Bulletin* 1943 v 40 386] and identified with the strain isolated by LIVESAY and POLLARD [this *Bulletin* 1944 v 41 209] in the same year from a patient diagnosed as suffering from Bullis fever has now been maintained by guinea-pig transfer through 22 generations. Using the lyophile technique the authors have found that this strain sometimes showed increased virulence and occasionally caused scrotal swelling in guinea-pigs. The human strain has been maintained for 15 generations the responses of inoculated guinea-pigs have varied from no reaction to definite febrile reactions often followed by short relapses.

The results are stated to be in conflict with those obtained at the Rocky Mountain Laboratory where a tick strain of the same origin was found to immunize guinea-pigs against American Q fever. The authors' strains showed no immunological relationship to this disease they were also unrelated to the rickettsiae of Rocky Mountain spotted fever or of scrub typhus.

Five human volunteers were inoculated with the human strain derived from the lyophilized tissues of infected guinea-pigs two of the subjects developed leucopenia (3 700 and 4 800 leucocytes per cmm) all had a relative lymphocytosis four developed fever in one the incubation period was 10 days fever of an intermittent type lasted 10 days the temperature rising to 99° or 100° F in another there were five spells of fever each of one day's duration over a period of 14 days. The type of fever in the other two patients is not mentioned.

Three volunteers were inoculated with the tick strain—one of them developed fever ranging from 99° to 100°F for the first six days; the temperature was then normal for six days and rose again for the last five days of the illness.

In 1944 two strains of rickettsia-like bodies were isolated from *A. americanum* ticks—the first from a pooled suspension of 1,850 ticks and the other from a suspension of 600 adult ticks. The guinea pig reactions were of the same general type as those obtained with the strain of the previous year. The first strain, after passage through a Berkefeld N filter, caused fever lasting 1–3 days in 5 out of 10 inoculated guinea pigs after incubation periods ranging from 6 to 12 days. The other strain could not be maintained in guinea pigs though filtered suspensions caused fever in three out of six guinea pigs after incubation periods of 3, 5 and 11 days. Unfiltered suspensions of this strain failed to cause a reaction in any of the five guinea pigs that were inoculated.

Better results were obtained with the next series of guinea pigs inoculated with the unfiltered tick suspension. Infection was transferred for nine generations—about half of the guinea pigs had fever of moderate or high intensity after an incubation period of 5–15 days, and inclusion bodies and rickettsiae were found in smears from the lungs.

Among 16 guinea pigs that had recovered from infection with this (1944) strain, 15 failed to react when inoculated with the tick strain isolated in the previous year; whereas among 10 controls two died and six others had febrile reactions.

[Final judgment on the infecting agent or agents in Bullis fever seems to be unjustified. Only one strain of rickettsia has yet been isolated from a patient and there appear to have been many failures. From the local ticks several strains of the same type have been isolated by the authors who however refer to the isolation of a tick strain of American Q fever from the same locality, and STEDRAUS and PARKER (this *Bulletin* 1945 v 42, 375) have isolated two strains of unidentified filter passing virus from rabbit ticks in the area. More than one short tick-borne fever may have been included under the name Bullis fever.]

John W. D. Megaw

YELLOW FEVER.

HECHT O & ANDRUE P. J. Contribución al conocimiento de la fauna Culicidiana de la parte norte de la Guayana Venezolana. [A Contribution to Information on the Culicidae of N. Venezuela.] Reprinted from *Boletín Entom. Venezolana* 1944 Sept. 30 v 3 No. 3 105–18 [16 refs.] English summary

[This paper was abstracted in this *Bulletin* 1945 v 42, 465 where a reference is made to a table of 22 species of mosquitoes associated with the investigation of yellow fever. It was recently noticed, during the compilation of a list of blood-sucking arthropods used in yellow fever transmission experiments, that the table referred to contained some errors.]

The authors reproduced a table of 22 species of mosquitoes which was compiled by STEDRAUS and published in "Virus and Rickettsial Diseases" 1939 Harvard University Press, Cambridge, Mass. U.S.A. This gives the names of mosquitoes found naturally infected with yellow fever virus, those shown to be able to transmit it by biting, and those in whose bodies the virus has been shown experimentally to persist for various periods. They have marked with an asterisk those species in the list which are known to occur in Venezuela, and those found in the present investigation with a double asterisk. Five of the

mosquitoes in SIMONS's list however appear to have been included by mistake they are *Wyeomyia bromeliarum* *W. obliqua* *Limatus durhami* *Anopheles albitalis* and *Anopheles tarsimaculatus*. The results of the experiments made with these mosquitoes by DAVIS and SHANNON (this Bulletin 1931 v 28 727 1932, v 29 197) were negative and no later experiments at least with a different result appear to have been made see also the list given above p 609

The following species were collected by the authors *Anopheles argyritarsis* *A. osculdoi* *A. psaloi* *A. rangeli* *Wyeomyia quasiluteoventralis* *Sabethes belisarii* *S. cyaneus* *S. purpureus* *S. imperfectus* *Psorophora champerico* *P. cyanescens* *P. ferox* *P. litzi* *P. discolor* *P. onfimus* *Haemagogus celeste* *H. equinus* *H. spegazzinii* (syn *janthinomys capricornis*) [see note to Table III above p 609] *Aedes aegypti* *A. leucoclaenus* *A. hastatus* *A. scapularis* *A. serratus* *A. fluviatilis* *A. terreus* *A. upatensis* *Mansonia fasciolata* *Culex brevispinosus* *C. chidestery* *C. corniger* *C. coronator* *C. conservator* *C. declarator* *C. educator* *C. maracayensis* *C. mollis* *C. quinquefasciatus* [*C. fatigans*] *C. surinamensis* *C. theobaldi* *Aedomyia squamipennis* *Uranotaenia pulcherrima* *Megarhinus trinidadensis* total 42 species

J F Corson

DENGUE AND SANDFLY FEVER.

GILBERTSON W E Sanitary Aspects of the Control of the 1943-1944 Epidemic of Dengue Fever in Honolulu. *Amer J Pub Health* 1945 Mar v 35 No 3 261-70 4 figs

The author who is a Public Health Engineer gives a vivid account of the energetic and thorough measures of control that were adopted in Honolulu to prevent dengue from becoming a threat to military efficiency

The infection, which had been absent from the area since the 1912 epidemic, appears to have been introduced by aircraft pilots coming from the Fiji Islands in July 1943. In spite of prompt measures of control by the local Board of Health the disease continued to spread and there was a danger of an explosive outbreak so that the help of the U.S.A. Public Health Service was enlisted. By Sept 15 a staff of 96 persons was at work. Each man was provided with a kit consisting of a supply of kerosene Paris green and phenothiazine larvicides a flashlight and mirror for inspecting water containers chalk to mark arrows on sidewalks record sheets pamphlets of instructions to householders, a pipette and phials for collecting larvae.

All premises were inspected and dealt with every 10 days by squads of about six men with a foreman and records were made of all breeding grounds of mosquitoes. Special attention was paid to water pockets in various plants and trees. Although more than a million inspections of premises were made ground pools with earth sides were found to contain *Aedes* larvae on only four occasions. Adult mosquitoes in and round the houses were dealt with by pressure hand sprays. A crew of 30 men removed 3 600 truck loads of cans bottles etc. Roof gutters were removed or perforated, tree and rock holes were filled with cement all plants harbouring water were removed, and where suitable pools were stocked with *Gambusia affinis*.

The spread to other islands was controlled by spraying all departing aeroplanes and by local spraying in any locality in which a person coming from Honolulu later developed dengue.

The pupils of schools were enlisted as volunteers—they detected 30 000 water containers and found larvae breeding in 5 000 of them. The local Press, wireless broadcasts, cinemas posters and leaflets, were extensively used in an educational campaign.

A sharp reduction in the incidence of the disease followed the use of these measures, and a crippling epidemic was prevented. Less than one per cent. of the inhabitants were attacked, and very few cases occurred among the military personnel. Imported and sporadically occurring cases continued to be found so that it was necessary to persist in the precautions.

Aedes albopictus was undoubtedly a vector but it seemed to be less effective than *Aedes aegypti*. For effective control, it appeared to be necessary to reduce the *Aedes* index to a much lower level than that found effective against yellow fever.

John W. D. Meyer

FRANCISCO R. Is there Phlebotomus Fever in Puerto Rico? *Bol. Asoc. Med. Puerto Rico* 1944 Dec v 36, No. 12, 506-11

Two cases of short fever in Porto Rico lasting about two and four days respectively are suspected by the author to have been of the sandfly-fever type because of their short duration and the absence of rash or lymphadenopathy. The author mentions that there had been a recent epidemic of mosquitoes and there was no evidence of the occurrence of sandflies.

[In the circumstances dengue fever seems to be a much more likely diagnosis.]

John W. D. Meyer

PLAGUE.

WITLIN B & WILBAR, C. L. Jr Effect of Penicillin on experimentally produced Plague in Guinea Pigs. *J. Lab. & Clin. Med.* 1945 Mar v 30 No. 3 237-43

A comparison of the mortality of plague in the three areas, Hamakua District of Hawaii, San Francisco and New Orleans, shows an extraordinary figure for Hamakua of 89.1 per cent. and for the other two of 49 and 32 per cent. respectively. The Hamakua mortality 110 deaths among 111 cases from 1910 to 1944 is given as a reason for using this area for studies of plague. Penicillin treatment naturally suggested itself and the test animal was the susceptible guinea pig. The result was wholly disappointing whether the penicillin was inoculated before at the time of or after the inoculation of 2,500 *P. pestis* organisms and whether the organisms were inoculated intraperitoneally, intramuscularly or subcutaneously. All the guinea pigs died.

W. F. Harley

ABRAMOVA, S. G. [The Opsonic Index as a Test of Immunity to *P. pestis*.] *Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii* Moscow 1944 No. 10-11 72-6. [In Russian.]

The author has investigated the value of the opsonic index for detecting the presence of immunity after vaccination against plague. Citrated blood was added to a *Pasteurella* suspension and incubated for 30 minutes—a stained film was then made and the average number of organisms in one leucocyte was estimated. Thirty-six guinea pigs were immunized with a living culture of an avirulent strain of *P. pestis* and the opsonic indices were then determined.

In 16 animals a value of 10 or more was found (maximum 26.2) in 11 animals 5-10 and in 5 animals 1-5. Eleven unvaccinated controls all showed values less than 1. In animals vaccinated with a virulent culture the opsonic index began to rise two days after infection, and reached 55 after 9-13 days.

Twenty-eight immunized guinea-pigs were given a test inoculation of virulent *P. pestis*. Correspondence between the degree of immunity and value of the opsonic index was not exact: thus—index less than 1: 3 animals, all survived; 1-5: 4 animals, all survived; greater than 5: 21 animals, 18 survived. The value of the opsonic index observed bore no relation to the virulence of the strain of *P. pestis* used in the test.

D. J. Bauer

CHOLERA.

LAHIRI S. C. Sulphaguanidine, Sulphathiazole and Extract of Suprarenal Cortex in the Treatment of Cholera. *J Indian Med Ass* 1945 Mar v 14 No 6 113-15

A considerable body of evidence is now accumulating to show the value of sulphaguanidine in cholera. Stress is laid on the necessity, as in all bacterial infections, of early treatment. Once cholera is fully established, treatment resolves itself into combating severe dehydration and accompanying depletion of salts and colloids and their effects. Suprarenal cortex hormone is said to control the sodium metabolism and water balance of the body, and this was the good reason for its use in a few grave cases of the present series. Altogether 315 patients were admitted to hospital, of whom 114 were treated with sulphaguanidine, 25 with sulphathiazole and 176 with calomel. Due attention has been paid to the importance of age distribution for comparison of each series, but if we leave this out of count and take simply the total deaths as index to efficacy, we find that the percentages were 14.9, 29.5 and 28 for sulphaguanidine, calomel and sulphathiazole respectively. The dosage of sulphaguanidine was somewhat lower than has been recommended, which was itself an attempt to lower the expense of treatment without sacrificing efficacy. On this basis the dose used was 1 gm. initially, repeated at two-hourly intervals for two more doses, and then at four hourly intervals to give the patient a total of 5 gm. in 24 hours. Later the initial dose was increased to 2 gm. with successive doses of 1 gm. as before, and total dose in 24 hours up to 6 to 7 gm. The extract of suprarenal cortex in the form of eucortone was given intravenously, 2 cc. at a time, in 100 cc. of 25 per cent. glucose, followed by saline transfusion, and was thought to have good result.

W. F. Harvey

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

COHEN L. & HARRISON Irene. Gastric Function in Amoebic Dysentery. *South African J Med Sci* 1945 Feb v 10 No. 1 27-30

It has often been stated that the hydrochloric acid of gastric juice acts as a barrier against infection with *Entamoeba histolytica*. The authors have investigated this matter but on the grounds that the estimation of gastric acidity is a very unreliable indicator of gastric function, subject to considerable variation, they have done so by means of the neutral red excretion test. In this 5 cc. of a 1.0 per cent. solution of neutral red is injected intravenously.

and the time of first appearance of the dye in the aspirated stomach contents, and the time of maximum concentration, are noted. In normal persons the neutral red appears within nine minutes, and is at the maximum in 6-20 minutes after injection.

Twenty five persons all presenting the clinical criteria of dysentery and 11 of whom cysts of *E. histolytica* were found, were tested by this method. The results were within the range of normality except in four subjects of whom two showed definite hypo-excretion, and two were slightly subnormal. These results show that amoebic dysentery may and usually does, occur in the presence of normal gastric function, and that gastric anacidity cannot be regarded as a significant factor in the etiology of amoebic dysentery.

Charles Wilcocks

BROWN, R. L. Evaluation of Techniques used in the Diagnosis of Enteric Protozoism in Children. *J Lab & Clin Med* 1945 Feb v 30 No 2, 135-7

By the use of four techniques (saline films, iodine films, dry slide stained with iron-alum-haematoxylin, and concentration) the author was able to determine 648 specific parasites among 512 children (ages 6 weeks to 12 years) examined. The frequencies in percentages were as follows: —*E. histolytica* 8.0, *E. coli* 33.2, *E. nana* 30.5, *D. fragilis* 3.9, *I. bilis* 1.4, *G. intestinalis* 32.2, *C. mesnili* 5.1, *Embryonated intestinalis* 2.3, *Trichomonas hominis* 1.4, *Ascaris lumbricoides* 0.6, *Enterobius vermicularis* 4.1, *Trichuris trichiura* 0.4, *Taenia* sp. 1.2. Of these parasites it was possible to identify the species by the use of simple saline films in 80 per cent of cases. By the use of iodine films the species were identified in 33 per cent. of the remainder. The stained film was most instructive for by its use 96 per cent. of all the parasites found could be identified. Concentration methods were most useful for detecting parasites which would otherwise have been missed. By their use the total number of parasites found by other methods was increased by 11 per cent.

C. W. Wexler

RELAPSING FEVER AND OTHER SPIROCHAETOSIS.

SLAVINA, N. S. On the Carriage of Spirochaetes of Tick-borne Relapsing Fever by Tick Vectors in Kazakhstan. *Med Parasit & Parasitic Dis* Moscow 1944 v 13 No 5 85-7 3 figs. [In Russian.]

Having established the occurrence of tick-borne relapsing fever in Kazakhstan (Central Asia) the author carried out a series of tests with 306 "wild" ticks (*Ornithodoros papillipes*) with a view to determining their rôle as carriers of the spirochaetes. In the course of these experiments the ticks were allowed to feed on guinea-pigs which were subsequently examined for the presence of spirochaetes both directly (thick drop method) and by subinoculation of other guinea-pigs (no diagnosis). The infection rate among the ticks was found to be 3.4 per cent., as compared with 2.2 per cent. established for the same locality in 1940. It is pointed out that the feeding method used for the detection of infected vectors is not always reliable for occasionally ticks failed to infect guinea-pigs through the bite, whereas an emulsion of their teased-up guts produced infection. It is, therefore, thought that the infection rate among the ticks is actually higher than the figures given above and that an increase in the incidence of relapsing fever among human beings might be expected in the area in question.

C. A. Hoare

BASU B C. & SEN S Experimental Studies in Rat-Bite Fever *Indian Med Gaz* 1945 Feb v 80 No 2 82-4

The authors report the course of the disease in various laboratory animals infected experimentally with *Spirillum minus*. Out of 44 guineapigs 5 died before showing any signs of infection the remaining 39 became infected. The period of initial attack when spirilla first appeared in the blood, varied from 1 to 49 days the average being 10.3 days and up to 3 relapses were observed. The disease does not seem to produce febrile symptoms in these animals but there was loss in weight after the organism appeared in the blood. The 44 guineapigs lived from 6 to 101 days the average being 37.2 days.

Thirteen white rats were inoculated intraperitoneally with infected blood, and 10 became infected after incubation periods of 3 to 17 days. The initial attack lasted from 1 to 6 days and up to 6 relapses were observed. The infected rats lived from 9 to 170 days the average being 63.1 days. Three of the rats were refractory to repeated inoculations.

Twelve white mice were also inoculated two died 2 to 3 days later the remaining 10 became infected after an incubation period of 4 to 6 days. The initial attack lasted for 1 to 34 days the average being 12.1 days and up to 3 relapses were observed. The infected mice lived up to 120 days the average being 34 days.

One kitten was inoculated intraperitoneally and became infected on the 11th day. Its blood remained positive for the next 10 days after which the animal died. Another kitten fed on infected blood remained free from the disease.

Culex fatigans fed on infected white mice showed no signs of *S. minus* in the gut within 24 hours and the organisms were never found in any other part of the bodies of the mosquitoes. Similar results were obtained with rat fleas although in these insects the spirilla in the gut were still motile after 24 hours.

E Hindle

YAWS

RIFKIN H Yaws in a White Soldier *Bull U.S Army Med Dept* 1945 Mar No 86 81-3

A white soldier in the tropics got a splinter wound in the finger and in five weeks an ulcer developed there. A month later acute lymphangitis of the arm with enlargement of the epitrochlear and axillary glands developed. Microscopical examination showed the presence of spirochaetes resembling *Spirochaeta pertenuis* and from this evidence and also the appearance of the ulcer a diagnosis of yaws was made. The Kahn reaction of the blood was strongly positive but the cerebrospinal fluid was normal. A biopsy of an enlarged lymph gland was made and showed spirochaetes. He was given injections of mapharsen in doses of 0.06 gm. (except the first two injections) twice a week for 11 injections (0.615 gm.) and three injections of bismuth. After the third injection of mapharsen the Kahn reaction became negative and remained so and after the fifth injection the healing of the ulcer was complete. J F Corson

LEPROSY

FAGET G. H. & POGGE, R. C. Penicillin Treatment of Leprosy. Clinical Note. *Pub Health Rep* Wash. 1945 Mar 23 v 60 No. 12, 324

"Penicillin was tried at the National Leprosarium in the treatment of 7 cases of leprosy in doses of 50 000 to 100 000 units daily which were continued in some cases for a month a time. No specific beneficial effect could be attributed to this treatment either during the course of medication or for 6 months thereafter.

Subsequently two of the previously treated patients and two new patients were given much larger doses of penicillin without effect.

HELMINTHIASIS

GRAM ELOISE B. JONES, MYRNA F. & WRIGHT W. H. A Potential Intermediate Host of *Schistosoma mansoni*. *Science* 1945 Mar 23 302

There is no record of a human being having acquired schistosomiasis in the United States of America, and none of the known snail hosts exists there: recent experiments by the authors however appear to indicate that a local species of snail, *Tropicorbis aeneus* is susceptible to infection with *Schistosoma mansoni*.

The snails were laboratory reared progeny of specimens collected from a lake at the edge of the campus of the Louisiana State University: they were exposed to miracidia of *Schistosoma mansoni* in the "water of the finger-bowl aquarium," and cercariae began to emerge from one of the snails a month later. Two other snails of the same species were afterwards infected.

J. F. Corson

ALMY T. P. & HARPER J. G. M. Banti's Syndrome apparently due to Infection with *Schistosoma mansoni*. *J Amer Med Ass* 1944 Nov 11 v 128, No. 11 703-5 4 figs.

An interesting record, chiefly on account of the disease being a medical curiosity in the United States. The patient was an Arab born near Aden in 1899 leaving there at the age of fifteen and having lived in the United States since 1919. He gave a history of diarrhoea and the passing of blood when 14 years old. Except for a winter cough he was in excellent health till 1941 when his spleen was found to be enlarged. After that he became weak and lost weight, and swelling of the abdomen and legs appeared, with dyspnoea on mild exertion. On admission (1943) the mucosae were pale, liver hard, but not tender 7 cm. below the costal margin at mid-clavicle line, spleen to the umbilicus: there was moderate oedema of ankles and over the tibiae. Red corpuscles numbered 3,600,000, leucocytes 4,000 per cmm., with 12 per cent. eosinophiles. After three weeks on iron and liver extract the red cells numbered 4,900,000, leucocytes were still 4,000 but the eosinophiles were down to 4 per cent. Faecal examination revealed scanty ova of *S. mansoni*. Foulsm was given but there was no change in the spleen, the liver or the blood count, except that the eosinophiles rose to 25 per cent. to fall again to 7 per cent. Strength improved and the oedema disappeared. A point of special interest is the chronicity of the disease and the long interval during which the patient seems to have been quite well, for it is almost certain that he had been infected 30 years before [see also this *Bulletin* 1945 v 42, 47].

H. Harold Scott

MAZZOTTI L. Datos sobre la cisticercosis en México [Cysticercosis in Mexico]
Rev Inst Salubridad y Enfermedades Trop Mexico 1944 Dec v 5
No 4 283-92 2 figs [30 refs] English summary (2 lines)

In the two and a quarter years December 1936-March 1939 among 128 025 pigs slaughtered 5 558 (4.34 per cent.) were measled. In 1938 LABARDINA found eggs of *Taenia* (species not stated) in 2 per cent. of over 4 000 human faecal specimens others have recorded their presence in 1.1-2.7 per cent. of those examined. Cysticercosis was found in 13 among 450 autopsies at the Guadalupe Civil Hospital and in the period March 1938-April 1944 ROBLES operating upon 100 cases of cerebral tumour found 25 due to cysticercosis. Ocular cysticercosis is said to be far from uncommon it has been found in 2.8 per cent. of autopsies in the City of Mexico. Auto-infection is suggested by the fact that in 63 examinations with the perianal swab 44 revealed ova of *T. saginata* [this *Bulletin* 1945 v 42 134] one patient with *T. solium* was positive on two successive days then negative on three days. Of another 131 examinations by the swab 108 were positive (*T. saginata*) and ova were also found elsewhere on the body the lumbar and hypogastric regions and on the underclothes. It has been noted that the proglottides of *T. solium* do not emerge spontaneously as do those of *T. saginata* but only with the faeces. Man would appear to be more susceptible to infestation by ova of *T. solium* than by those of *T. saginata* this is fortunate seeing that the latter may be present sometimes in large numbers in the perianal and other regions of the body.

H Harold Scott

CAUSEY O R DEANE M P DA COSTA O & DEANE L M Studies on the Incidence and Transmission of Filaria, *Wuchereria bancrofti* in Belém Brazil. *Amer J Hyg* 1945 Mar v 41 No 2 143-9 6 figs. on 2 pls

Belém in the State of Pará Brazil, has long been known as an endemic centre of filariasis and *Culex fatigans* abounds there. Though this mosquito is common in other parts of the Amazon Valley filariasis is not. The present study is based on detailed investigation of 14 parasitized individuals and on a general survey of 5 000 persons examined. Blood samples taken three-hourly from eight patients showed that embryos might be present in considerable numbers from 9 p.m. to 9 a.m. with a peak at midnight. Of six others bled hourly from 6 to 9 p.m. and thereafter three-hourly all contained microfilariae between 7 p.m. and 3 a.m. five were positive at 6 a.m. three at 9 a.m. and two at noon.

Next collectors visited houses in various parts of the city observed any cases of elephantiasis and took thick blood films from persons to include all ages and in as nearly equal proportions of both sexes as was possible. Five thousand in all were examined. The results are detailed in the letter press but the table reproduced gives the information very clearly and will save a long description. The great difference in the existence of elephantiasis recorded among males as among females is explained by the authors statement that the true rate was not obtained because elephantiasis is more easily concealed in men and much of the data was collected by non medical assistants. The reader must therefore bear in mind that columns 7 8 11 and 12 are to be taken with this reservation and columns 9 and 10 are also not quite accurate though less inaccurate than the others. column 11 gives the incidence of microfilariae among cases of elephantiasis and column 12 the incidence of elephantiasis among cases of filariasis.

The incidence of microfilariae in the blood was observed to increase with age the youngest positive was a two-year-old boy and the youngest with elephantiasis a boy of eleven years. Of 841 under ten years of age 54 (6.4 per cent.) showed microfilariae whereas of 2 762 aged 20 years or over 346 (12.5 per cent.) showed the embryos in their blood.

Among more than a thousand *C fatigans* captured in Belem and examined 11.6 per cent were found infected. This is by far the commonest mosquito there. Of more than half a million mosquitoes collected from 1 641 houses (the average per house was 334) between January and July over 99 per cent were *C fatigans*. Of 563 specimens of *A darlingi* examined three were found naturally infected with filaria larvae and of 332 specimens of *A aquasalis* two were infected. Three other species of *Anopheles* *A oswaldoi* *A triannulatus* and *A albistarsis* were infected experimentally but were not found infected in nature. Since *C fatigans* breed well in polluted water the first thing to do in the way of prevention is to improve the general sanitation and give due attention to the sewerage and drainage systems.

H Harold Scott

GARRATT E I Clinical Filariasis due to *Acanthocheilonema (filaria) persians*
Trans Roy Soc Trop Med & Hyg 1945 Mar v 38 No 4 287-90

Infection with *Acanthocheilonema persians* appeared to be the cause of the symptoms observed in two natives of Northern Nigeria reported in the present paper. One patient was admitted to hospital complaining of pain in the upper part of the abdomen diarrhoea and vomiting. There was deep tenderness in the epigastric area and the edge of the liver was four fingers breadth below the costal margin. There was no jaundice or muscular rigidity. As no cause could be found, a course of emetine was started, but in the early morning of the third day after admission the patient complained of severe pain and showed signs of shock. The liver was explored with a needle. blood only being withdrawn, and this was found to contain an excess of polymorphonuclear leucocytes and numerous living larvae of *A persians* though none were found in the peripheral circulation. Laparotomy was performed but there were no signs of liver abscess. Emetine administration was discontinued after 6 grams had been given and the patient slowly recovered. he was in hospital for 25 days.

The second patient also had upper abdominal pain but no other symptoms. He had had several previous attacks. There were a few larvae of *A persians* in the peripheral blood. The liver was explored with a needle blood being withdrawn and found to contain many larvae of *A persians*. He was given a course of anthiomaline and the number of microfilariae in the liver blood diminished greatly. He was discharged recovered 36 days after admission and had no recurrence during three months after discharge.

Both patients had a negative Kahn reaction and both had hookworm ova in the faeces but they seemed to cause no bad effects except a moderate degree of anaemia and hookworms are very common in the native population.

J F Corson

NOTE ON THE DISTRIBUTION OF ONCHOCERCIASIS IN MEXICO
Dr Frederic C BARTTER Medical Officer in Charge Onchocerciasis Investigation Pan American Sanitary Bureau has asked that the following note be published

Numerous textbooks of tropical medicine and parasitology and numerous articles on onchocerciasis contain the statement that onchocerciasis exists in the state of Guerrero Mexico

"Actually the disease has never existed in that state being confined at present to the states of Chiapas and Oaxaca. The error arose through a confusion of names between the township of Montecristo de Guerrero in the state of Chiapas and the State of Guerrero.

The first communication in the literature dealing with this subject appears in the *Boletín de la Salubridad Pública de México* in 1926, where it is stated that the township of Montecristo de Guerrero in the Department of La Libertad, in Chiapas contains 4,000 cases of onchocerciasis.

In 1928 Charles HARDWICKE in *Trans Roy Soc Trop Med. and Hygiene* (XXI No. 6) quotes (citing reference) the above report. In Montecristo de Guerrero State of Chiapas 4,000 cases etc. However in his summary in the same article he gives origin to the error thus, "its course can be traced along the mountain range of the Sierra Madres, with infected areas in these mountains from the Guatemalan frontier through the states of Chiapas, Oaxaca and Guerrero."

In 1930 Carlos C. HOFFMANN published a map of Chiapas, in which the township of Montecristo de Guerrero was indicated prominently and in the accompanying text (*Archiv für Schiffs und Tropenhygiene* 1930 v 34 461-472) he correctly places the township in La Libertad, in Chiapas.

However in the same year Hoffmann delivered a lecture before the Seventh Latin American Congress in which he said "We still lack grounds to establish whether this focus (i.e. the focus in Montecristo de Guerrero Chiapas—Ed.) is in any way related to the isolated infected regions in Oaxaca, (Larumbe 1926) or with infected portions of Guerrero (Hardwicke 1928)." He thus carries on the error of Hardwicke.

Subsequently as stated above the error has become prevalent in numerous books and articles.

The author has been assured by Dr. Salvador Gonzales Herrejón, director of the campaign for the control of onchocerciasis of the Mexican Government that no authenticated case of onchocerciasis has been reported from the state of Guerrero. Although the state of Guerrero borders that of Oaxaca the onchocerciasis zone in the latter state is relatively confined, and is not known to extend further west than the city of Oaxaca itself.

"The author is indebted to Dr. Eduardo Caballero for the use of his reprint library including several unpublished works of Carlos C. Hoffmann.

DEFICIENCY DISEASES

H. C. & Dju M. Y. Riboflavin Deficiency among Chinese. 3. Urinary excretion of Riboflavin. *Chinese Med J* Washington D.C. 1944 Apr-June v 62 No 2, 140-51.

Riboflavin excretion studies were made upon a group of out-patients visiting the nutrition clinic certain hospital in-patients a group of healthy middle school and college students, healthy hospital staff and others.

"Among 32 healthy students the mean value of urinary riboflavin in 24 hours was 147.5 ± 68.8 9 hospital staff 186.1 ± 125.2 9 other healthy individuals 167.6 ± 101.3 . The majority of them gave a percentage excretion value of 10 gammas per cent or more. There appears to be a direct correlation between the peloid or nutrition index and the riboflavin excretion.

Among 41 patients showing eye signs of riboflavin deficiency 23 or 56.1 per cent. showed zero or only a trace of riboflavin in the urine the mean value of urinary riboflavin was 27.4 ± 23.5 which was considerably lower than

the values for normals given above. This is in contrast with a group of 10 patients showing eye signs of avitaminosis A whose mean value for urinary riboflavin was 100.9 ± 49.1

A low urinary riboflavin value was also obtained among a group of 29 patients showing cheilosis and glossitis. The mean value was 39 ± 27.9

The percentage excretion values among ariboflavinoses cases was lower than those of normals. Most of the patients gave a value of 5 gammas per cent

The urinary excretion of riboflavin increased immediately after an increased intake through the diet or by the administration of pure riboflavin. When the dosage was large and the administration was continued for a number of days a greater portion of riboflavin was excreted through the urine.

In many patients showing low riboflavin excretion there were usually found a low vitamin B₁ and a low nicotinic acid excretion. In the majority of cases both before and after treatment the excretion of riboflavin ran parallel to the vitamin B₁ excretion. The amount of riboflavin excreted was usually in proportion to the urinary volume.

The daily estimation of riboflavin excretion is an aid in the diagnosis and in estimating the degree of riboflavin deficiency

Hou H C. Riboflavin Deficiency among Chinese. 4. Glossitis. *Chinese Med J* Washington D C 1944 Apr-June v 62 No 2 152-65 4 figs [11 refs]

One hundred and thirty-six cases of glossitis of riboflavin deficiency were observed and treated.

The outbreak occurred during the winter months of 1941 to 1942 involving mainly young people of ages from 18 to 30 years in institutions where the diets were deficient in vitamin B complex

Painful tongue was the main symptom. The tongue usually showed patches of bluish red and magenta red discoloration with flattened papillae or scattered prominent papillae. The majority showed furrows of various degrees. Other symptoms and signs frequently occurring were sore lips, dry throat and cheilosis. Pericorneal injection of the eye was seen in a number of cases while blepharitis and seborrhoeic dermatitis were seen each in two cases. Associated deficiencies of vitamin B₁ and vitamin A although mild were seen in the majority of the cases

The urinary excretions of riboflavin and vitamin B₁ in the cases tested were below normal. The percentage of riboflavin excretion was about 5 mg per cent. in all but one.

Glossitis rapidly subsided following treatment with riboflavin. The dosage used was 4.5 mg daily for the first two days and subsequently 2.3 mg daily

The possibility that glossitis is due to a riboflavin deficiency associated with a mild degree of nicotinic acid deficiency is discussed

HAEMATOLOGY

HYNES M, ISHAQ M & MORRIS T L. Iron Deficiency Anaemia in North-West Indian Soldiers. *Brit Med J* 1945 May 5 626-8.

A haemoglobin survey was performed on some 1 400 soldiers native of North West India during the spring of 1944. All the subjects were physically fit and of upwards of one year's service

Widespread mild anaemia was found the mean haemoglobin level being 13.42 gm per 100 ml. Only one-third of the men had over 14 gm and 14 per

cent. had less than 12 gm. Red cell counts and haematocrit determinations on 341 selected cases revealed that the anaemia was always hypochromic and either normocytic or less commonly microcytic thus suggesting that it was due to iron deficiency.

Stools were examined for hookworm ova, but the results indicated that hookworm infestation did not usually accompany the mild cases of anaemia, although in most of the more severe cases infestation was present.

A number of the men were treated with iron in heavy dosage for periods of two or three weeks, with consequent marked improvement in the haemoglobin levels in the anaemic cases whether hookworm infestation was present or not.

The average daily food ration of these soldiers was found to contain over 60 mgm. iron but of this all except 1 mgm. was derived from vegetable sources.

The authors conclude that most of those cases not due to hookworm infestation were due to inadequate iron intake the greater part of the dietary iron presumably not being assimilated, possibly owing to the effect of phytic acid or mineral imbalance on the absorption of iron from the cereal diets.

L. J. Davis

ALTMANN A. Sickle Cell Anaemia in a South African-Born European. *Clin. Proc. Cape Town*. 1945 Jan-Mar v 4 No. 1 1-10 4 figs. [20 refs.]

Sickle cell anaemia has been described but very rarely in the white race. Altmann records the case of a 24-year-old male white South African who manifested the features of this disease. The patient suffered repeated attacks of fever jaundice pains in the limbs and joints cardiac murmurs and a cerebral vascular accident.

Haematological and biochemical studies indicated a haemolytic anaemia. Examinations of the erythrocytes revealed increased resistance to hypotonic saline the presence of many target cells and pronounced sickling in wet sealed preparations.

The patient's parents were born in South Africa, and the paternal grandparents came from Scotland. Two of the patient's sisters showed the sickling trait. As a young child the patient was diagnosed as syphilitic and given appropriate treatment. In adult life he had slightly kinky hair a flattened nose a markedly mongoloid face and a coffee-coloured skin. But these appearances are considered by the author to be features of the disease rather than suggestive of coloured blood (?).

L. J. Davis.

VENOMS AND ANTIVENENES

BOQUET P. Recherches physio-pathologiques et immunologiques sur le venin de dendraspes [Studies on *Dendraspis* Venom.] *Rev. d'Immunologie* Paris. 1944-1945 v 9 No 1-2, 31-8, 1 fig. [15 refs.]

There are several species of *Dendraspis* in Africa. *D. viridis*, *D. jamesoni*, *D. angusticeps* and *D. antinorii*. As their name implies they are tree-dwellers. They are quick and aggressive, striking at the face, neck, arms and chest of passers in the forest. Though belonging to the proteroglyph Colubridae they have, like the Viperidae, a mobile upper jaw for erecting the fangs. Experiments were carried out with rabbits guinea-pigs and mice and two species of *Naja* and one of *Sepeidon* were used for comparison. The m.l.d. in the rabbit are shown in the accompanying table from which it will be seen that *N. tripudians* venom is four times as toxic and that of *N. ferox* 5-8 times.

Venoms studied	M.L.d. by intravenous injection, expressed as mgm. per kilo body weight
<i>Dendraspis viridis</i> Dakar 1940	0.8
<i>Dendraspis viridis</i> Dakar 1941	0.7
<i>Dendraspis angusticeps</i>	0.5
<i>Naja tripudians</i>	0.2
<i>Naja flava</i>	0.15
<i>Sepeodon haemachates</i>	0.5

The venom kills by causing paralysis and slow asphyxia. It lowers the blood pressure independent of the nervous centres. The venom of *D. viridis* possesses an anticoagulant property equal in potency to that of *N. tripudians* that of *D. angusticeps* is 50 times as potent.

Similarities between the symptoms and effects of *Dendraspis* venom and those of other Colubridae render it probable that they possess antigenic factors in common which would be neutralized by *Naja* antiserum (for therapeutic purposes). The author's researches led him to conclude that the venoms of *D. viridis* and *D. angusticeps* act like those of other African Colubridae and of the Indian cobra, but dose for dose the last is the more toxic. That of *D. viridis* however lowers the blood pressure (in rabbits) whereas that of *D. angusticeps* is strongly anticoagulant. In preparing polyvalent antivenenes for West and Equatorial Africa it would be wise therefore to add an antiserum (prepared from the horse) against *Dendraspis* as well as against *Bitis* and *Naja*.

H. Harold Scott

DEL POZO E. C. ANGULANO L. G. & GONZÁLEZ Q. J. Acciones del veneno de alacrán sobre el sistema vaso-motor [The Action of Scorpion Venom on the Vasomotor System.] *Rev. Inst. Salubridad y Enfermedades Trop. Mexico* 1944 Dec. v 5 No 4 227-40 4 figs. [19 refs.] English summary

The mode of action of scorpion venom has not been satisfactorily worked out. BERT in 1865 observed a low and widely varying arterial pressure in dogs receiving injections of the venom and WILSON in 1904 reported an early and marked increase in pressure succeeded by a gradual fall. AXIUS in 1913 and HOUSSAY in 1919 declared that the increased pressure was peripheral in origin, whereas MAGALHÃES in 1935 concluded that it was by central action and indirectly by the adrenaime secretory activity of the bulb.

There may be quantitative differences in the venoms of different species of scorpions but qualitatively they seem to be alike. The authors have carried out several series of experiments on cats under varying conditions: some anaesthetized with dial, some decerebrated, some with the medulla severed or encephalon destroyed, some with the adrenals extirpated or their action eliminated by ligation of their pedicles. The venom prepared from telsons of the *Centruroides suffusus suffusus* was injected into a femoral vein. The dose was 100 d.c.l. (dosis ciertamente letal i.e. the dose causing certain death of an 18-20 gm. mouse in 15-30 minutes.) The general effects were fibrillar and spasmodic contractions of the skeletal muscles, mydriasis, erection of the hair and marked salivation and death by respiratory paralysis. Vasomotor effects the chief subject of this study were an early rise of blood pressure observed in 11-12 seconds succeeded by a gradual fall during 8-10 minutes occasionally longer and if small repeated doses were injected the initial rise was more prolonged. This rise is shown to be due chiefly to stimulation of the sympathetic neurons.

proximal to the ganglia acting in part by way of the vasoconstrictors and in part by stimulating the adrenals. At the same time a cyclical type of respiration set in with prolonged periods of apnoea. The initial rise of pressure was observable even in decerebrated animals and in those whose adrenals had been removed or ligated. If the sympathetic nerves to the ears were severed, the adrenals being left intact vasoconstriction occurred, but not if the adrenal action was cut off nevertheless the action is not on the adrenals directly because if the glands are left intact but the spinal cord is destroyed, the vasoconstriction does not occur. If the vagi are intact inoculation of the venom is followed by bradycardia but not if these nerves are severed.

H. Harold Scott

DERMATOLOGY AND FUNGUS DISEASES

PARSONS, R. J. & ZARAFONETIS C. J. D. Histoplasmosis in Man. Report of Seven Cases and a Review of Seventy-One Cases. *Arch Intern. Med.* 1945 Jan. v 75 No 1 1-23 5 figs. (Numerous refs.)

This article is an important contribution to the study of histoplasmosis and should be read in the original.

During the twenty years following DARLING's discovery in 1905 of histoplasmosis in Panama, no other report of the occurrence of this disease was made until RILEY and WATSON in 1929 [this *Bulletin* 1927 v 24 68] described a case in the United States and their report was quickly followed by others. In 1932, DE MOYRETT (*Amer. J. Trop. Med.* 1934 v 14 83) succeeded in cultivating the causative fungus *Histoplasma capsulatum* and from this time onward the number of cases reported annually in the United States has greatly increased and the disease has been recognized in Brazil, Central America, Java, England, Argentina, Mexico, Rhodesia, the Philippines and Austria. The marked increase in the number of reported cases is not attributed to an actual increase in the incidence of the disease but to greater accuracy in diagnosis.

The authors give a tabulated analysis of 71 cases, 56 collected from the literature and 15 hitherto unpublished. They also describe in clinical and pathological detail, 7 cases which came under their personal observation and three other cases. There is no indication of the source or mode of infection. The fungus has never been found vegetating saprophytically in nature but the disease has been identified on three occasions in the dog and a yeast-fungus bearing a resemblance to *Histoplasma* has been seen in the tissues of a mouse and a ferret. Histoplasmosis occurs sporadically and persons of all ages are susceptible. In a series of 60 cases 11 were in infants under 1 year old. The white race has provided the great majority of the patients and the disease seems to be commoner in males than in females. There is no known occupational predisposition but agriculture has provided more patients than any other calling. The disease may attack any organ of the body and all have been involved in some case or another. It may be limited to a single tissue such as the adrenal glands or several tissues may be affected, and the clinical signs and symptoms will depend on the distribution of the lesions. The lungs are often affected and pulmonary tuberculosis may be simulated, or it may even co-exist with the histoplasmosis. Ulcerating granulomata, frequently met in the mouth, pharynx, larynx or intestine, may suggest malignant disease or tuberculosis and the frequent general enlargement of the lymphatic glands and the spleen may lead to the diagnosis of leukaemia or Hodgkin's disease while histoplasmosis of the adrenals may be reflected clinically only in the signs of adrenal insufficiency. In

three cases *H capsulatum* caused vegetative endocarditis affecting the auriculo-ventricular valves and in one of these cases the diagnosis of subacute bacterial endocarditis had been made

The diagnosis of histoplasmosis depends on the identification of the fungus in microscopical preparations or in culture from the lesion and the most useful material for this purpose is morbid tissue obtained by biopsy. The parasite may sometimes be found in smears of the peripheral blood or sternal bone marrow but diagnosis should not be made dependent on this method of examination alone. Inoculation of morbid material into an animal susceptible to the infection, such as the mouse rat or guinea pig may be used when the material is too grossly contaminated for direct culture tests. Dermal hypersensitivity to filtered extracts of cultures of *H capsulatum* may prove an aid to diagnosis.

The prognosis for the disease is almost invariably fatal. Treatment has not proved effective but there seems to be some promise of usefulness in radiotherapy and in drugs of the antimony group

J T Duncan

SCHLUMBERGER, H G. A Fatal Case of Cerebral Coccidioidomycosis with Cultural Studies. *Amer J Med Sci* 1945 Apr v 209 No 4 483-96 9 figs [17 refs]

A fatal case of disseminated coccidioidomycosis is reported in which the outstanding lesions were found in the brain. Fifteen additional examples of intracranial infection by the fungus are listed. The organism was isolated and both mycelium and spherules grown in culture using the roller tube apparatus of Gey. Hamsters were very susceptible to the fungus frogs were refractory. Neither in the patient nor in the experimental animals was there evidence of mycelial growth

KUNSTADTER, R. H. & PRENDERGRASS R. C. Primary Coccidioidomycosis a possible Pediatric Problem. *J Amer Med Ass* 1945 Mar 17 v 127 No 11 624-7 1 fig [13 refs.]

IRIARTE D. R. Consideraciones sobre Paracoccidiosis. Observaciones del Servicio de Otorrinolaringología del Hospital Vargas [Paracoccidiosis.] *Bolet Laboratorio Clinica Luis Razetti* Caracas 1945 Feb v 13 No 16 277-85 6 figs

[*Paracoccidioides* of which there are several species known produces a granulomatous condition which may be local or more generally distributed. It occurs chiefly in South America and particularly in Brazil. The species more concerned in the generalized forms are *P. tenuis* and *P. brasiliensis* with the localized form *P. caryophylli*. The first cases seen in Venezuela were discovered by O Daly in 1937 in post mortem examinations and the first in a living body was one described by the author and RODRIGUEZ in 1939 [the author makes this statement but does not give the reference] in a patient with lesions localized to mouth and larynx. In this form the lips are infiltrated thickened and hard and the mouth is invaded tongue palate pharynx and larynx. Some authorities maintain that the lungs are first involved and the upper passages and the mouth secondarily but the majority favour the idea of the mouth lesion being primary and the lung involvement (when it occurs) as secondary.

The author gives brief notes of two cases. The first was in a negro 32 years of age who stated that ten months before coming to hospital he noticed ulceration at the left angle of the lower lip. Later the upper lip and the gums became involved for six months his voice had become hoarse and he had difficulty in swallowing. The epiglottis was infiltrated and ulcerated as were

the arytenoids. A biopsy specimen of the epiglottis showed the lesions to be paracoccidiodial granulomata. Sulphapyridine was given the lesions cicatrized, the infiltration subsided, the hoarseness and dysphagia disappeared. [The dosage is not stated beyond that "38 pastilles were given.]

The second case was very similar. The patient was a white man of 61 years, who had had ulceration of the upper lip for a year. Later the palate, hard and soft, was invaded. He had been hoarse for three months and had had difficulty in swallowing for 2½ months. Examination revealed ulceration of the right nostril, the palate, epiglottis and arytenoids. Biopsy proved the cause. This time sulphathiazole was given, "120 pastilles or 60 grammes" and, as in the other patient, ulcers cicatrized and the symptoms cleared up. Radiograms are reproduced designed to show the condition on entering the hospital and after treatment but are not very clear.

H. Harold Scott

MISCELLANEOUS DISEASES.

FAIRLEY \ H. Medicine in Jungle Warfare. *Proc. Roy. Soc. Med.* 1945 Mar & 38 No 5 193-8 (Sect. of Epidem. & State Med. 13-16)

During six months' campaign in the Huon Peninsula and the Markham Ramu Valley in New Guinea, the chief diseases were—malaria (60.5 per cent.), dengue (17.5 per cent.), dysentery and diarrhoea (6.5 per cent.), scrub typhus (2.5 per cent.) and skin and other diseases (13 per cent.).

Bacillary dysentery was spread chiefly by polluted water. The administration of sulphaguanidine lowered the incidence and severity of the disease and "it is now only possible to isolate dysentery bacilli in approximately 10 per cent. of diarrhoeal cases admitted to hospital. Sulphaguanidine was very effective in the severe epidemic among the Australian soldiers fighting over the Owen Stanley Ranges in 1942—the epidemic was controlled within 10 days. The drug is expensive but it is absolutely safe for field use—no toxic symptoms of any importance occurred, there was no anaemia even in dehydrated patients and the fatality rate of treated cases is 1/5,000.

Scrub typhus.—"This is the only disease which is killing troops with regularity in the south-western Pacific area"—the average case mortality is about 8 per cent.—but it varies in different areas from 0 to 30 per cent. apparently owing to variation in the virulence of the rickettsiae. For preventive measures di-butyl phthalate is more persistent in clothing after immersion in water or washing, than di-methyl phthalate. When wearing treated clothing (socks, trousers and shirt) it is possible to be down in country swarming with mites without getting a single bite. Blankets also require treatment. Mites causing scrub itch are not necessarily concerned with scrub typhus.

Scrub typhus is restricted to small areas, often widely separated, so cases should be reported promptly and the suspected area put out of bounds. No specific treatment is known.

Dengue though not fatal, causes much incapacity among troops. *Aedes scutellaris* is a vector in New Guinea—it breeds in rain water in casual receptacles—tins, coconut shells, &c.—and in the axils of branches of mango trees—it bites in the daytime and appears not to fly further than 200 yards. Experiments on volunteers confirmed that *Aedes scutellaris* is a vector and failed to incriminate *Anopheles brevis* and *Aedes aeneus*. Antimosquito measures were effective.

Malaria.—"Throughout the Milne Bay and Buna-Gona campaigns in 1942 malaria casualties far exceeded battle casualties—the hospital admission

rate in three to four months almost equalling the total strength of the Forces involved. In these campaigns suppressive treatment consisted for the most part of quinine grains 10 daily. Later in 1943 there were very heavy malaria casualties in the Ramu and Markham Valley and the Huon Peninsular campaigns when the suppressive drug regime consisted of 0.1 gramme of atabrin (mepacrine) daily on six days of the week.

A research centre was established in Northern Queensland to test the value of all known antimalarial drugs. Volunteers took the drug before, during and for 23 days after exposure to infection by bites of infective mosquitoes. Quinine 10 grains daily did not protect against infection with *Plasmodium falciparum* by 10 bites of *Anopheles punctulatus* var *typicus*. Fever with parasites in the blood always occurred within the usual incubation period, but fever and parasites disappeared with doses of 50 grams of quinine daily.

Quinine in 10 gram doses daily suppressed benign tertian fever in two-thirds of the cases while 5 grains failed. Atabrin however was found very effective. 0.1 gm daily or on six days of the week was taken before, during and for 23 days after the last infective bite. Benign tertian fever thus was suppressed but it always appeared 14 to 44 days later and parasites appeared in the blood 19 to 46 days later. Subtertian fever was also suppressed with the same dosage and did not appear later nor did the injection of 200 cc. of the blood of the bitten volunteers infect others. Infection was not prevented, because subinoculation from the 7th to 10th day infected other volunteers and since other tests showed that the bitten volunteers were susceptible it is concluded that they were infected and cured. Mixed infection with *P. vivax* and *P. falciparum* was also suppressed, even when exhausting conditions—fatigue, cold, anoxia, loss of blood—were present. About 30 days later however every volunteer developed benign tertian malaria but no subtertian parasites were found.

Confirmation of these results has been obtained in the Field. The admission rate to hospitals in New Guinea fell from 740 per 1 000 per annum in December 1943 to 28 per 1 000 in November 1944. Other factors—less fighting and mosquito control—also contributed to the good health record.

J. F. Corson

MASTER, A. M. Medicine in the South Pacific. *U.S. Nav. Med. Bull.* 1945 Feb. v. 44 No. 2 308-15

The author landed on one of the Solomon Islands in December 1943 at the beginning of the rainy season. The shade temperature was 85°-90°F and the relative humidity was 80 per cent. The annual rainfall of the Solomon Islands is said to exceed 160 inches.

Malaria control had already been established and mosquitoes were not numerous. Prefabricated steel buildings were erected by the medical staff, roads constructed and a water supply established, the work being done in mud which was sometimes 3 feet deep.

Among non-tropical diseases upper respiratory infections—acute pharyngitis, acute tonsillitis, acute tracheitis and acute catarrhal otitis media—were common. Prompt treatment with sulphadiazine enabled the men to continue working. Primary atypical pneumonia also occurred and was easily distinguished from lobar pneumonia by X-rays and by its mild clinical course. Diarrhoea was also common and was successfully treated with sulphadiazine or sulphaguanidine both being effective. Only four cases of amoebic dysentery were diagnosed.

Various skin affections—cuts, abrasions, prickly heat, impetigo, tropical ulcers and fungous infections—were common. Here also sulphadiazine proved

very effective. Pubic lice were troublesome at first, but were easily controlled by the aerosol bomb.

Malaria.—There were 500 cases of malaria in the first 3½ months, practically all being benign tertian—thick films only were used for diagnosis. There were no cases of blackwater fever. Treatment with atabrine [mepacrine] was effective but there were many relapses.

Typhus.—Cases of mite-borne typhus were admitted from neighbouring islands—the illness was severe and convalescence slow.

Worms.—Hookworm was common, about 10-20 per cent. of the Marines who had been in the jungle for six months or more being infected, while 80 per cent. of natives in the labour battalions had hookworm ova in the stools. There were two cases of infestation with *Strongyloides stercoralis* and in one the larvae were found in the sputum. *Diphyllobothrium latum* and *Hymenolepis diminuta* were also seen, and there was one case of larva migrans due to the cat or dog hookworm.

Organic heart disease was rare but tachycardia, as a symptom in the "effort syndrome," was common. J F Corson.

I. BALLY P R O *Catha edulis* *East African Med J* 1945 Jan. v 22 No. 1 2-3.

II. CAROTHERS, J C. Miraa as a Cause of Insanity *Ibid* 4-6.

i. Miraa is one of several local names (others are mirug, Lhat, cafta) of a tree (*Catha edulis*) usually some 20 feet in height, occasionally three to four times this, indigenous in Africa. Its leaves and twigs may be chewed, or infused as Bushman's Tea, or smoked, or the leaves may be made into a sweet with honey. It induces, particularly when chewed, a happy and mellow friendliness and an increased intellectual vigour and acuity. It is not a narcotic—in fact addicts suffer from insomnia.

ii. The author describes two cases of mental disturbance in addicts to this drug. The first patient was a male Somali, approximately 20 years of age admitted in an excited, aggressive state—in two days he was quieter but garrulous and was well enough to be discharged after 11 days. A little more than a week later he was re-admitted with similar symptoms accompanied by haughtiness, excessive politeness and grandiose hallucinations. This time he was four weeks in recovering. Nearly five months later he was again under observation with like symptoms, but this time recovery was not complete for 3½ months.

The second patient was a man of 30 years who was seen in four attacks at brief intervals. In his case recovery was more rapid—13 days, 4 weeks, 2 weeks and 12-13 days respectively. [Nothing is said regarding treatment if any was adopted.] H Harold Scott

HEISCH R. B. A Case of Poisoning by *Catha edulis*. *East African Med J* 1945 Jan. v 22, No 1 7-9

The author records a fatal case of poisoning by *Catha edulis*. This contains three known alkaloids—cathine, cathinone and cathidine. Except that it is not an analgesic the action is very like that of *Erythroxylon coca*. Chewing it causes excitement diminishes the sensation of fatigue allays hunger and induces addiction. The author states that only the green stalks are used and that the dried plant is probably inert but an editorial [see below] and a brief note by Dr BALLY [see above] in this issue of the *East African Medical Journal* state that the leaves and twigs are chewed and the dried leaves smoked.

The patient in the present record was an elderly Arab admitted in an excitable inarticulate condition with spasmodic movements of the limbs the pupils were normal in size and reacted to light and convergence but sluggishly. Legs and arms were spastic [but deep reflexes were not exaggerated] he was hypersensitive to sound and hyperaesthetic. Gastric lavage removed a large quantity of stalks of the plant. His temperature was 101°F but no malaria parasites could be seen. Two days after admission he passed into coma for which no cause other than the poison plant could be found and two days later he died without recovering consciousness [There is unfortunately no account of any post mortem findings or even of an autopsy being made]

H Harold Scott

EAST AFRICAN MED J 1945 Jan. v 22 No 1 9-10 The Need for the Control of Khat.

This is a short editorial on the subject of the cultivation of *Catha edulis* and its control. The question is not altogether a simple one because some people regard it as a harmless stimulant and compare it with alcohol. But alcohol is not so readily obtainable by irresponsible natives and is too expensive to be the cause of harmful addiction. On the other hand, the plant is grown or can be cultivated on a large scale and is thus easily obtained—in fact it is hawked around in towns—it soon engenders addiction and leads to mental disturbances and as Dr HEISCH has described (see above) perhaps to a fatal result. The consumption of it is increasing in East Africa and its harmful effects are becoming recognized something therefore should be done officially to stop or at least control its cultivation and use. Ten years ago a resolution was passed to this end by the Maru Native Council and more recently by the Isolo Native Council, making it an offence to possess the plant but for all the effects these resolutions have had they might be a dead letter. It is now suggested that its cultivation should be limited and that its sale should be restricted to a few persons under a licence. Absolute prohibition of the drug would seem to be inadvisable for various reasons writes the Editor [but these reasons are not stated]

H Harold Scott.

WRIGHT F J Haemoglobinuria in Typhoid Fever East African Med J 1945 Jan v 22, No 1 24-8

GENERAL ENTOMOLOGY

BULL. U.S. ARMY MED DEPT 1945 Mar No 86 13-14 Composition of Insecticides containing DDT

Information is given regarding the composition and uses of nine preparations of D.D.T. insecticides. Nos. 1 and 2 are powders containing 10 per cent. of D.D.T. in pyrophyllite [an aluminium silicate] no 1 put up in 2-oz. tins for personal use against lice in clothing no 2 in 5-lb. containers for mass delousing. No 3 is 100 per cent. D.D.T. powder in 10 lb. containers for dissolving in suitable oils to make 5 per cent to 0.5 per cent. D.D.T. sprays for use as insecticides or larvicides. No 4 is a powder containing 10 per cent. of D.D.T. in talc [magnesium silicate] for use it is diluted with an inert dust to make a 2 per cent. D.D.T. dust for areas where mosquitoes breed. No 5 is a 5 per cent. solution of D.D.T. in kerosene for use primarily in fly and mosquito control but can also be used against other insects it can be applied either by a spray

or a paint-brush. No. 6 contains 1 per cent. of D.D.T. and 2½ per cent. of thanite in refined kerosene for use in a slit-gun type of sprayer. No. 7 contains 6 per cent. of D.D.T. 68 per cent. of benzyl benzoate 12 per cent. of benzocaine and 14 per cent. of "Tween-80". It is diluted with 5 parts of water to form a spray for body lice and for scabies. No. 8 contains 3 per cent. of D.D.T., 2 per cent. of pyrethrum (20 per cent. extract) 5 per cent. of cyclohexanone 5 per cent. of hydrocarbon oil and 85 per cent. of "Froon 12". It is contained, under pressure, in 1 lb. steel cylinders fitted with a release valve, and is for use against mosquitoes and other biting flies. No. 9 contains 25 per cent. of D.D.T. 10 per cent. of "triton X 100" and 65 per cent. of xylene. It is used for impregnating underwear and will keep it louse-proof for some months through 6 or 8 ordinary launderings. For use it is diluted with 11 parts of fresh or sea water to make a 2 per cent. emulsion. *J. F. Corson*

BUSHLAND R. C. EDDY G. W. & KRIEPLING E. F. Tests with Synergists for Pyrethrum against the Body Louse. *J. Econom. Entom.* 1944 Aug. v 37 No. 4 558-7

Three pyrethrum synergists known to be effective in fly sprays were added to a pyrethrum louse powder and have proved to be effective. The synergists concerned were sesame oil DHS activator (ethylene glycol ether of pinene) and IN930 (N isobutyldodecylamide). The testing method involved applying 3.0 gm. of a pyrophylite powder (aluminosilicate) containing the insecticidal ingredients to the inside of a sleeve made of heavy cotton underwear material. Twenty-five young adult lice were placed in the sleeve, which was then fixed on the host's arm with adhesive tape. After twenty-four hours the surviving lice were counted. Twelve tests on each powder showed that 0.25 per cent. pyrethrins on pyrophylite gave a kill of 68 per cent. with 2 per cent. of synergist added the kills were—with IN930 100 per cent. with DHS activator 94 per cent., and with sesame oil 94 per cent. Pyrophylite containing 2 per cent. synergist alone was non-toxic to lice. It was later found that powders containing 2 per cent. IN930 and 0.01 per cent. pyrethrins or more were completely lethal to lice. Dusts containing only 0.005 per cent. pyrethrins plus 2.0 per cent. IN930 have given 100 per cent. kills in a number of tests with 0.25 per cent. IN930 the kill was about 68 per cent. It was concluded that 2 per cent. IN930 increased the toxicity of pyrethrins in the dusts by about one hundred times.

It was found that powders containing 1.0 per cent. pyrethrins remained effective for four days' wearing, and that this period was extended to eight days for a dust containing 0.2 per cent. pyrethrins and 2 per cent. IN930.

W. A. I. David.

KRIEPLING E. F. & DOVE W. E. Recent Investigations of Insecticides and Repellents for the Armed Forces. *J. Econom. Entom.* 1944 Aug. v 37 No. 4 477-80

The shortage of pyrethrum and rotenone coupled with an increased war time demand, stimulated the search for insecticides suitable for controlling insects and other arthropods of medical importance notably body lice, mosquitoes, houseflies, sandflies, fleas, mites and ticks. The work described can be divided into two main projects (1) body louse control, (2) repellents for use against various biting insects.

Louse control—At first a powder for individual application was preferred. Pyrethrum and rotenone and also several hundred synthetic organic compounds were tested. The early tests showed that pyrethrins and rotenone impregnated

on pyrophyllite were about equally effective but that pyrethrins were preferable since rotenone was slower in action and frequently caused scrotal dermatitis. It was found that the pyrethrum synergist isobutylundecylenamide (IN930) known to be effective in fly sprays increased the effectiveness of the pyrethrum louse powder also and was superior for this purpose to 300 other compounds tested [see also BUSHLAND EDDY and KNIPLING above]. The addition of 2 per cent. IN930 to the powder made 0.2 per cent. pyrethrins in the dust superior to 1 per cent. pyrethrins without activator. Later 2,4-dinitroanisole was added as an ovicide. The final formula known as MYL contained 0.2 per cent. pyrethrins 2 per cent. IN930 2 per cent. 2,4-dinitroanisole and 0.25 per cent. Phenol S (the latter as an antioxidant) in pyrophyllite. The powder was also effective against the crab louse (*Phthirus pubis* L.) and the head louse (*Pediculus humanus humanus* L.).

Repellents—The main emphasis was on the development of mosquito repellents which would be superior to citronella oil. Some of the early preparations were effective but also toxic however after extensive tests with *Aedes aegypti*, *Anopheles quadrimaculatus* and also *Stomoxys calcitrans*. Three effective and safe repellents were found—dimethyl phthalate, Rutgers 612 and Indalone. These three substances do not provide equally effective protection against the various species tested. Dimethyl phthalate proved to be a good flea repellent. Indalone was one of the more effective repellents against flies but was of little value against *A. quadrimaculatus* for the latter insect dimethyl phthalate was most effective. Rutgers 612 repelled *Aedes aegypti* most effectively. The period of complete protection against *Aedes* given by the three repellents ranged from three to five hours. When applied to clothing they prevented biting through the treated fabric for about one week. The duration of protection however depended greatly upon the conditions of the test on perspiring subjects for example it was much shorter.

All three repellents gave good protection against chiggers (*Eutrombicula* and *Acariscus* spp.) for short periods when applied to the legs and arms. The preferred procedure however is to apply dimethyl phthalate as a barrier on the socks cuffs of trousers sleeves and other openings in the clothing through which chiggers could crawl. An application requires 1.5–2.0 ounces and remains effective for a week. Similar methods proved effective against larval and nymphal stages of the tick *Amblyomma americanum* but not against adults.

The fleas *Ctenocephalides canis* and *C. felis* were also repelled when the same three repellents were applied to the skin on clothing these substances gave more prolonged protection.

W A L David

BISHOPP F C. Insect Problems In World War II with special references to the Insecticide DDT. *Amer J Pub Health* 1945 Apr v 35 No 4 373–8.

A general account.

KAHN M C CELESTIN W & OFFENHAUSER W. Recording of Sounds produced by certain Disease-carrying Mosquitoes. *Science* 1945 Mar 30 335–6.

In this extremely interesting note the authors report their investigation of the sounds made by certain mosquitoes. They were led to this in the hope that sound could be used to attract mosquitoes to spots prepared with DDT and thus perhaps to avoid the necessity of indiscriminate spraying of buildings and the consequent destruction of insects which are rather beneficial than harmful. Records were made by means of modern electrical apparatus of sounds—audible and inaudible to the human ear and the authors have found that genus and species has tonal emanations so distinctive that they

distinguished, as can the sounds produced by males and females of the same species. These seem to be mating calls or warnings of danger or calls of anger. All the calls are within the cycle range of the human ear but some are far too feeble to be detected.

The noise of a single female will cause the males of the same species to burst into an answering chorus, and the males turn the antennae and hypopygium in the direction of the female. The sounds may be made when the mosquito is in flight, or by the beating of wings when it is resting or by the rubbing of tarsi against the wing, but there are certain pure hard-like sounds whose origin is not yet known.

The work is being continued.

Charles Wilcocks

GETTING V. A. Insect Vectors of Disease. *New England J. of Med.* 1945 Mar 15 2: & 29 v 232, Nos 11 12 & 13 315-21 344-50 373-8. [178 refs.]

PARROT L. & DE JOLIVIERE, P. B. Notes sur les Phlébotomes. XLVI Nouveaux Phlébotomes du Hoggar [New Phlebotomus in the Hoggar] *Arch. Inst. Pasteur d'Algérie* 1945 v 23 No 1 58-63 5 figs

LABORATORY PROCEDURES.

LILLIE, R. D. The Deterioration of Romanovsky Stain Solutions in various Organic Solvents. Purification of the Thiazins and Spectra of Purified Dyes. Spectroscopic Data on Paired Mixtures of Purified Thiazins and on Commercial Thiazins. *Suppl. No 178 to Pub Health Rep* Wash. 24 pp [Numerous refs.]

This is an account of spectroscopic examination of Romanowsky stains. In the first paper are recorded the results of an investigation of the changes that may occur in old solutions of Wright's stain—in watery solutions a shift of the thiazin absorption band away from the red end of the spectrum was noted as well as a relative decrease in this absorption band as compared with the eosin band. Solutions of various Romanowsky stains in various solvents were studied both at room temperature and at 55°C. or higher. The solvents were various alcohols glycols and glycerol. The findings are given in detail in the text and in tables in an appendix. "Solutions in ethanol and diethylene triethylene and dipropylene glycols are apparently more stable at room temperature than solutions in methanol, but at higher temperatures ethanol and methanol mixtures with 40 to 50 per cent. of glycerol were the only ones giving satisfactory stability. Solutions containing 1.2 gm. per 100 cc. in ethanol glycerol or methanol glycerol stain optimally in about half the time required by 600 mg./m 100 cc. solutions [the usual strength]." "Schiffner's granules are better shown in 1-hour staining at 1:50 dilution with 600 mg. 100 cc. solution in either solvent [methanol or ethanol with glycerol] than in standard Giemsa stains.

The second paper records an attempt to prepare pure samples of methylene blue, azure B, azure A, azure C and thionin, while in the third paper mixtures of these purified stains were examined "in an attempt to provide comparison standards for commercial and laboratory samples of these dyes." These dyes could not be prepared in the dry form so mixtures of the solutions were used. The results are shown in a table.

J. F. Corson.

BOOK REVIEWS

VARGAS LUIS. *Simulidos del nuevo mundo* [The Simuliidae of the New World.]
 Monografía Num 1 del Instituto de Salubridad y Enfermedades Tropicales
 241 pp 10 pls. 1945 Mexico D.F

The title of this book is a little misleading though not to the extent of being inaccurate. It contains two parts: the first is a summary of our knowledge of the biology, morphology, etc. of the Simuliidae; the second contains a summary of proposed classifications of the family, a catalogue of sub-families, tribes, genera and sub-genera proposed by various authors within the family and, finally, a catalogue of New World species. It must be emphasized that there are no keys or descriptions for the identification of species. The author's aim has been to collect available information and present it in a form easily distributed to workers concerned with onchocerciasis in Central America and Mexico; he is not presenting new results of his own investigations except incidentally; for original contributions by him have appeared in a number of papers elsewhere.

Much of the material in the first part that on biology, etc. consists of actual quotations from published work of other authors or re-statements of their findings and opinions. It would be invidious to start to comb through this part of the book and comment on these selections, especially as the reviewer is ignorant of the library facilities at the author's disposal; a few factual comments may however be made.

The reviewer notes that the work of the following authors is not mentioned: METCHNIKOW (*Zeits f Wiss Zool* 1866 v 16 392-406) in which the embryology of a simuliid is described in the careful descriptive style of the period; PULIKOVSKY (1927 *Zeits Morph u Oekol. Tiere* 1927 v 7 384-443 *ibid* 1929 v 13 655-664) and on the pupal respiratory organs; VOGLER (*Mitt. Schweiz Ent Gesell* 1887 v 7 277-282) on the pupal tracheal system; WAGNER (*Zool. Jahrb* 1925 v 12 441-486) on larval respiration; WILHELM (*Die Krisibel mückenplage* 1-246 1920 Fischer, Jena) summarizing our knowledge of the Simuliidae and which has a long and valuable (though occasionally inaccurate) bibliography; and WILHELM & SALING (*Zeits f Wiss Zool* 1928 v 132 329-354) supplementing and bringing up to date WILHELM's book and the bibliography therein.

The author adopts the nomenclature applied to the male external genitalia by GIBBINS (*Ann Trop Med Parasit* 1935 v 29 317-325). This is a pity; the nomenclature adopted by DE MEILLON (*Publ S Afr Inst Med Res* 1934 v 6 253-263 and 323-347 v 7 208-215 and 393-402) which closely resembles that of EDWARDS (*Dipt Pat S Chile* 1931 Pt 2, Fasc. 4 121-154) though perhaps not perfect is to be preferred. Some of GIBBINS's nomenclature in which he called the median structures posterior median and anterior phallosome seems to have been derived from Professor PATTON's use of these terms in his writings on external genitalia of Cyclorrhaphous Diptera. The simuliid genitalia should of course be compared in the first instance with those of other Nematocerous Diptera.

A few more figures—there is no figure of the entire adult simuliid fly!—would have increased the value of this first part of the book.

In the second part of the book the author begins with a summary of various classifications that have been proposed for the family but without presenting much critical comment upon the various segregates proposed. He accepts the simple classification proposed by EDWARDS (1931 *loc*) and as later modified by EDWARDS (*Arch Hydrobiol* 1934 Suppl. Bd. 13 92-138). He rejects the

classification of ENDERLEIN (*Arch Phylog Ent* 1930 v 1 77-97 and else where) with its multiplicity of genera. He rejects the recent classification of RUBTZOY (*Fauna de l'U.S.S.R. Insectes Diptères Fam. Simuliidae* 6(6) 1-532 1940) which is in its turn derived to a considerable extent from the Enderleinian system. He does not accept the classification proposed by TWIXX (*Canad Jl Res Sec D* 1936 v 14 97-150) for the North American fauna. There are useful tabular statements of the classifications of ENDERLEIN TWIXX and RUBTZOY.

In the catalogue of the sub-families tribes, genera and sub-genera which follows, the method of presenting the material is somewhat extended and it is doubtful if the extension succeeds in conveying much more information than would some of the more compact and space-economizing methods commonly in use amongst taxonomists. Three generic names are omitted *Miodania* Enderlein (*Tierwelt Mitteleurop* 1938 v 6 in Teil 2 Lief. xvi, 39) genotype, *M. opalinipennis* n. sp. (l.c.) *Simulidium* Westwood (*Qm Jl Geol Soc* 1854 v 10 384 and 394) genotype *S. priscum* n. sp. (l.c.) and *Pseudosimulium* Handlirsch (*Fossilien Insekten* 1908 Lf 4 631) genotype *S. humidum* Brodie (by designation of Handlirsch l.c.). The first genus was recorded in the Zoological Record of the year 1936 and its omission is regrettable the last two are fossil genera and it is not surprising that they have been overlooked. *Mallochella* Enderlein (1930 l.c.) is preoccupied by *Mallochella* Duda (*Arch Naturgesch* 1925 v 90 74) a genus of Borboridae.

The author gives particulars of *Atractocera* Meigen *Velusina* Meigen and *Eusimulium* Roubaud as though matters relating to these three genera were all straightforward they are not. The first two are still subject to a final decision amongst taxonomists as to what to do about misidentified genotypes the second is also subject to a final settlement of the vexed question of the Meigenian names of 1800 while the fixation of the genotype of the third is a matter of interpretation of the language employed by ROUBAUD when he first used the name in a sub-generic sense coupled with the use made of the name by DYAR and SHANNON (*Proc U.S. Nat Mus* 1927 v 69 (no. 2636) 1-54). The genotype of *Simulium* Latreille itself is erroneously given as *replans* Linnaeus the author quotes EDWARDS (*Bull Ent Res* 1915 v 6 23-42) as his authority for this statement. It is now generally agreed that Latreille's genotype *columbascensis* Fabricius is synonymous with *columbascense* Schönbauer and not synonymous with *replans* Linnaeus. A review is not the place to discuss this matter it will be taken up in a paper by the reviewer that is in the press (*Trans R. Ent Soc Lond*).

In giving in the final section, the catalogue of New World species the author has performed a useful service the last catalogue of North American species being that of DYAR & SHANNON (1927 l.c.) and of South and Central American species that of PIRIO (*7a Revue Soc Arg. Pat. Reg. Norte* 1932 v 60 661-763) a considerable number of new species have been described since then by various authors. It would have been helpful if the author had indicated new synonymy if any and the authorities for the old. One or two points struck the attention of the reviewer as he looked through this catalogue. *S. chilense* Philippi is given as a species and then immediately below where *S. chilinum* Rondani (or as some writers would put it *chilinum* Philippi in Rondani) is treated as a valid species, *chilense* Philippi appears as a synonym. It cannot be both the reviewer recently considered them distinct species (SMART *Proc R. Ent Soc B* 1944 v 13 131-136). Further on, *kirtipes* Fries of EDWARDS (1831 l.c.) is given as synonymous with *kirtipes* Fries of ENDERLEIN this is not the case and ENDERLEIN (*Zool. Anz* 1925 v 62, 201-211) proposed the name *myrtales* for the species that he maintained EDWARDS had, in many places misidentified as *kirtipes* Fries (SMART l.c.).

student that the recent outbreak of yellow fever in the Sudan indicated the danger of spread to the Far East where conditions would be very ripe for a disastrous epidemic. The authors state (p. 31) that "it is impossible to differentiate epidemic typhus, murine typhus and Rocky Mountain spotted fever by means of the Weil-Felix reaction since high OX19 titers may occur in all these diseases." This conflicts with the usual opinion that the reaction in the tick-borne rickettsial diseases is usually of low titre. A warning is rightly given that louse-borne typhus may be contracted by the inhalation of infected dust; it might have been added that there is a danger to the medical man of acquiring the disease during the process of taking blood for the Weil-Felix test. The bald statement (p. 48) that there is no specific treatment for Rocky Mountain spotted fever leaves out of account the promising American work on hyperimmune rabbit serum. An instance of the modernity of the information is the reference (p. 55) of the value of dibutyl phthalate in the prevention of tsutsugamushi disease.

Amoebiasis has become one of the major therapeutic problems of the war and current opinion is that success in treatment especially in chronic cases depends not only on the use of the right drugs but also on the observance of essential details in their administration and in the management of the patient. The description given by the authors of the various methods of treatment will not greatly help those dealing with difficult cases.

In the description of malaria a good impression is given of the complex subject of *Anopheles* transmission and a list of the chief vectors with their geographical distribution and habits occupies 6 pages. The only important species omitted is *A. vedderi* but there is reason for this as it has only recently been differentiated as a species from *A. gambiae*; nevertheless it was well known for many years as the black variety of *A. gambiae*. On page 248 it is stated that malaria can break through a routine of suppressive mepracrine in doses of 0.1 gm. daily in the presence of excessive fatigue, trauma and haemorrhage but there is very good evidence that this dosage is rarely adequate even under the most exacting conditions. The authors do not make the point that suppressive mepracrine can completely prevent malignant tertian malaria but that benign tertian is likely to occur after cessation of the suppressive routine.

In the section on leishmaniasis no mention is made of local infiltration of oriental sore with mepracrine, a treatment which has received much favourable note. In the treatment of African trypanosomiasis it is stated that lumbar puncture should be performed immediately but it would have been wise to say that the puncture should be postponed until the blood had been sterilised, so that the danger of introducing trypanosomes directly into the cerebrospinal fluid might be avoided.

For a book of this size the section on medically important arthropods is a long one: it comprises 143 pages of good material and it includes much advice on control. Medical officers in the field will appreciate this information. Another useful feature of the book is a good section on anthelmintics.

For the rest the binding and paper are excellent and the illustrations superb. Interesting and well drawn diagrams illustrate the important epidemiological points. There are very few misprints. Without qualification this book can be recommended to Service medical officers: the authors are to be congratulated on the results of their care and industry.

Charles Wilcocks.

TROPICAL DISEASES BULLETIN

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SUMMARY OF RECENT ABSTRACTS *

VII HELMINTHIASIS

[Continued from p 614]

Anthelmintics

BALDWIN (p 54) has devised a method for studying the action of anthelmintics on segments cut from the body of *Ascaris lumbricoides* of the pig. Certain substances including santonin, act chiefly on the anterior segment which contains the nerve ring and ganglia others including hexyl resorcinol thymol oil of chenopodium carbon tetrachloride and tetrachlorethylene act on both the anterior and the intermediate segments (which are regarded as nerve-muscle preparations free from nerve ganglia)

COLLIER and ALLEN (p 676) have found evidence that some of the soluble derivatives of phenothiazine accelerate the haemolysis of red cells which is produced by lysins such as saponin and lysolecithin. This accelerating effect may explain the haemolytic anaemia which occurs when phenothiazine is given to some species of animals

BEATTIE *et al* (p 409) have successfully treated a case of acute carbon tetrachloride poisoning by the administration of methionine. The rationale of the treatment was based on the knowledge that liver damage due to chloroform anaesthesia can be prevented in this way. It is thought that the cause of liver disturbance induced by carbon tetrachloride is abnormal metabolism of methionine and related compounds

Hookworm and Strongyloides Infection

LOWE and LANCASTER (p 950) report on a considerable number of men of the Australian army who returned from service in the islands of the north with hookworm infection. *Ancylostoma duodenale* *Necator americanus* and *A. brasiliense* were found, but the infections were light and the authors concluded that such anaemia as was found was caused rather by malaria than by the hookworms. The only blood change was an increase in the absolute number of eosinophil cells. For treatment the authors used tetrachlorethylene (4 cc) carbon tetrachloride (3 cc.) oil of chenopodium (2 cc) or hexyl resorcinol. In

The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1944 v 41. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

this dosage tetrachlorethylene constantly caused muscular inco-ordination, and the authors state that the doses quoted are maximal. MAPLESTONE (p. 951) comments on the paper by LOWE and LANCASTER to the effect that carbon tetrachloride is and should be regarded as a dangerous drug, a dose of 1.5 cc. having caused death on one occasion. Its toxicity is largely independent of the size of the dose and all the evidence goes to show that it invariably causes liver damage, whether there is clinical evidence of it or not. It has been superseded by tetrachlorethylene.

KRATZ and CRILLY (p. 139) claim that in infection with *Necator americanus* certain radiological appearances (called the 'deficiency pattern') may be detected, which cannot be attributed to other disease. This is much more apparent in those with clinically significant infection than in those with few incidental worms. Anthelmintic treatment leads to a return towards but not to the normal pattern in the former group. It may be worth noting, however, that persons with clinically significant hookworm infections are usually suffering from malnutrition also.

It has long been postulated that the anaemia of hookworm disease may be due not only to loss of blood but also to the effect of some toxin produced by the worms. HEILIG and LIVESTONAR (p. 499) remark that certain infections and states of malnutrition play a part in preventing the regeneration of blood, so that in these conditions even a few worms may precipitate the anaemic state but it is unlikely that there is any worm toxin which can produce aplastic anaemia. Heilig himself however thinks as a result of previous work that the cardiac complications of hookworm anaemia are caused in part by some factor other than anaemia, connected with the worms, and the authors have shown that perfusion of the heart of the frog with preparations of serum from patient with severe hookworm infection causes well marked reduction in the amplitude of the heart beat. They therefore postulate a factor toxic to the heart muscle which is not amenable to anti-anaemic treatment though its effect may be masked by the improvement caused by blood regeneration. This toxic factor is probably a toxin, not in the chemical but in the serological sense, and the authors note that antibodies have been found in the blood of dogs infested with *A. caninum*. The existence of an anti haemopoietic toxin has not been proved, and is improbable.

MACGREGOR (p. 949) has made a study of the bone marrow in the hypochromic anaemia found in hookworm disease. The appearances and also those found in examination of the peripheral blood suggest a dual deficiency of iron and (possibly) of the anti-pernicious anaemia factor, and analysis of the diets of the patients showed them to be very poor in iron, protein and in sources of the anti-pernicious anaemia factor. A remarkable improvement takes place in patients given massive iron therapy augmented by intramuscular injections of liver extracts. This paper emphasizes the importance of dietary deficiency in the production of hookworm anaemia. THAGARAJAH (p. 409) has found that the anaemia of women admitted to a lying in hospital in Ceylon is of the nutritional deficiency type—hypochromic and microcytic—and this he attributes to insufficiency of iron and to damage of the intestinal mucosa by hookworms. He therefore emphasizes the need for iron therapy after deinfestation by anthelmintics.

ARANGO (p. 1053) relates the anaemia so often found in association with hookworm infestation simply to the weight of that infestation, and supports the view that it is due to continued blood loss from lesions of the intestinal mucosa. [It will be remembered, however, that other workers have laid stress on the influence of faulty nutrition, as well as of blood loss, in the production of this anaemia.] The blood picture shows hypochromic, microcytic anaemia, with reticulocytes after administration of anthelmintics.

count falls but this does not happen if liver extract is given before and after their administration.

DE MEILLON and LAVOPIERRE (p 679) have produced creeping eruption by applying hookworm larvae (from S African dogs probably *A. braziliense* or *A. caninum*) to the skin. They think it unlikely that mites are the cause of similar eruptions. SMITH (p 680) has had success in treating creeping eruption with intramuscular Fouadin but BLANK (p 680) reports failure by this method.

WATT (p 766) has obtained evidence that rats infested with *Nippostrongylus muris* and placed on diets deficient in thiamin or riboflavin were less resistant to reinfestation than controls. Plasma from normally fed infected rats has a protective action when injected into other animals but plasma from these rats on deficient diet was not so effective.

LOWE and LANCASTER (p 951) have treated a number of men infected in New Guinea and the neighbouring territories with *Strongyloides stercoralis*. The symptoms included chronic cough, dyspepsia and chronic diarrhoea, without anaemia but with eosinophilia. In treatment gentian violet is disappointing though it relieves symptoms. Fouadin, tartar emetic and emetine failed to affect the stages of the worms in the tissues.

LEVIN (p 411) has given a general account of the clinical features of infestation with *Strongyloides stercoralis* of which he has seen 12 cases in Russia. The severity of the symptoms may be very varied—some patients show little sign of illness but in others the disease may be fatal or may suggest appendicitis or peptic ulcer. Details of the symptoms are given in the original abstract. Treatment was not very satisfactory; thymol gave the best results but gentian violet was not used. SHINIORALOVA and SEMENOVA (p 411) have studied 29 cases of infestation with *Strongyloides*; they describe the prominent symptoms and note that eosinophilia was usual. The treatment consisted of gentian violet or crystal violet given daily for 8–16 days. Symptoms showed striking improvement after this but in some cases larvae were found to persist. Much more study of this disease is needed.

By examination of the duodenal contents, CANÇADO (p 223) has found larvae of *Strongyloides stercoralis* in 9 per cent. of people in Belo Horizonte, Brazil. The infestation is especially prevalent among the poor.

Ascaris Infection

FERNANDO and BALASINGHAM (p 413) call attention to the fact that two-thirds of the population of Ceylon (of all ages) are infested with *Ascaris lumbricoides* and that there is a case mortality rate of 8 per cent. in patients with acute ascariasis. This acute condition is not rare, especially in children under 5. It is postulated that an infestation may give rise to acute symptoms because of toxic effects of products liberated when the worms die in the intestine. So many persons are infested but do not present the acute syndrome that some other factor than infestation seems to be concerned and infection of *Ascaris* material can cause the symptoms of acute ascariasis. The manifestations may be—acute inflammation of the alimentary tract (like infective diarrhoea), toxic and cerebral, sometimes simulating meningitis, acute abdominal symptoms of partial obstruction or simulating appendicitis, respiratory symptoms due to larval infiltration of the lungs or mixed symptoms. Treatment for these forms is outlined but for the details the original abstract should be consulted.

ARDAO and ZERBONI (p 767) point out that faecal examination may be negative for the eggs of *Ascaris lumbricoides* if the worms are all males or infertile females. A diagnosis may be made radiologically though a negative finding does not necessarily exclude ascariasis. The authors give an account of

the radiological appearances which may be seen after the ingestion of an opaque meal in *Ascaris* infection.

EARLE (p. 768) reports a case of asthma apparently due to infection with *Ascaris*.

BAUMANN (p. 859) records the case of a man with acute pulmonary symptoms pleural effusion and eosinophilia, who shortly afterwards began to pass eggs of *Ascaris* in his faeces. The author thinks that the syndrome was probably due to the larvae of the worm, in the pulmonary stage of their development and in this connection, discusses Löffler's syndrome. SOMMER (p. 680) expresses the view that Löffler's syndrome of pulmonary infiltration and eosinophilia may be allergic in nature and that the allergic state may be due to infestation with *Ascaris*. The pulmonary lesion may be due to larvae of the worm in a sensitive person, and the author in fact proposes the name eosinophil anaphy lactic pneumonia for this condition. He quotes cases in support of his view especially one in which the symptoms cleared up quickly after expulsion of a single male worm and in which the allergic state to *Ascaris* antigen was very marked, so much so that intradermal injection of the antigen led to typical anaphylactic shock.

BRUNNER *et al* (p. 952) have investigated the subject of skin sensitivity to antigens prepared from *Ascaris* in dogs infested with various intestinal nematodes. For details the reader should consult the original abstract.

LOZANOV (p. 140) reports favourably on the use of hexylresorcinol : infestations with *Ascaris lumbricoides*. TRIM (p. 596) has studied the action of hexylresorcinol on *Ascaris lumbricoides* and finds that the main path of entry into the tissues of the worm is through the cuticle. Results of a study of the uptake of the drug by the worm in the presence of biological substances such as are found in the alimentary tract are given in the original abstract. Bile salts tend to inhibit the uptake but may have a different effect *in vivo* because of the interference of other components of the complicated emulsion in the small intestine and because the drug is adsorbed to mucus.

OLIVER-GONZÁLEZ (p. 223) has studied the action, on larvae of *Ascaris lumbricoides* of the pig of antibodies in the sera of rabbits infected with *Ascaris* eggs or infected with extracts of the whole adult worms. These antibodies cause the formation of precipitates round the orifices and cuticle of the larvae and also immobilize and kill a large proportion of them. Extracts of isolated issues of *Ascaris* did not provoke the formation of such potent antibodies.

OLDHAM and WHITE (p. 789) have shown in pigs that the condition known as white spot liver can be produced by feeding the animals with embryonated eggs of *Ascaris lumbricoides*. The distribution of the lesions in the liver indicates that infection is conveyed by the portal vein and not by way of the peritoneal cavity.

Filaria

In the *Bulletin of the U.S. Army Medical Department* (p. 860) there was published an account of filariasis in troops in the Pacific Islands. It is noted that the earliest onset of symptoms occurred 3 months after arrival and consisted of lymphangitis, swelling of the glands or acute inflammation of the scrotum, testis and spermatic cord. No microfilariae were seen in the blood, but adult worms were found in some biopsy material. Intradermal tests were positive in the majority of the patients, but were also positive in a few controls. It is evident that signs and symptoms can develop very soon after exposure to infected mosquitoes.

DICKSON *et al* (p. 303) have investigated filariasis in the natives of the Samoan islands and in American soldiers there. Infection is present in a high proportion of the islanders, and a considerable number of Americans have been infected.

Failure to find microfilariae in the blood does not exclude the condition. Acute lymphadenitis or lymphangitis may be the earliest sign of filariasis usually in the arm or leg but there is a highly characteristic scrotal lesion with funiculitis. There is a tendency to multiple involvement and recurrence but there are no severe constitutional symptoms. Skin tests with an antigen prepared from *Dirofilaria immitis* were positive in the large majority of patients tested. The authors think that there is not much chance of recurrence in patients repatriated to the United States and that the disease should not prove a serious disability. Treatment consists of rest and reassurance—drug therapy has so far failed.

BURHANS *et al* (p 599) give a detailed list of the symptoms and signs found in men of the United States Navy who had returned from the South Pacific diagnosed as suffering from lymphangitis. Though no parasites were found the men were thought to be suffering from filariasis and nearly all had lymphatic gland involvement. Details should be sought in the original abstract. Sulphonamides were not useful in treatment but X ray therapy promptly brought about decrease in the size of the glands. It is not yet known if this is a permanent effect.

NEUMANN (p 854) describes filariasis as it affects white persons in the Samoan Islands. Symptoms may be absent even with heavy infection or they may be allergic (with oedema) or due to streptococcal infection (with fever and lymphangitis) or to staphylococcal infection (with local pain or abscess). Repeated attacks of streptococcal infection lead to elephantiasis. This infection is amenable to sulphonamide treatment whereas the staphylococcal infections are not. Microfilariae are not found in the blood in the early stages of filariasis and diagnosis must rest on the clinical symptoms. After leaving the endemic areas white men are usually free from these attacks.

MICHAEL (p 956) makes the point that in several thousand blood examinations on men of the United States forces infected with *Wuchereria bancrofti* in the Samoan region he failed to find microfilariae. Most of the men developed symptoms 7-9 months after exposure to infection and most had lymphangitis and funiculitis. Skin tests with an antigen prepared from *Dirofilaria immitis* were positive in 87 per cent. In 36 of 120 specimens removed at biopsy living or dead adult worms were found. These were in the peripheral lymphatics or lymph nodes. It seems that spontaneous recovery takes place after the patient leaves the endemic area. FLYNN (p 956) reports similar findings.

LOWMAN (p 600) has found microfilariae of *W. bancrofti* in the blood of an infant aged 14 months in a South Pacific island and argues that the early appearance of filariasis in American troops in that area is possible and that this should be borne in mind by medical officers.

CLEARKEIN (p 598) notes that the absence of microfilariae from the blood is not evidence of the absence of filariasis and that a positive Fairley skin test may be accepted as confirmation of diagnosis. Pathological changes may be the result of blockage of lymphatics infection or allergic reactions for the latter the author is experimenting with desensitization methods using extracts of *Dirofilaria immitis*. This treatment promises to be useful. Streptococcal vaccines have also been used with some success.

HARTZ (p 955) gives a detailed description of the histological appearances in the granulomata found in the lymphangitic lesions of filariasis. Details should be sought in the original abstract but a mistake in the abstract should be corrected. It is stated that there is no necrosis and little eosinophilia if the microfilariae are alive but that large numbers of eosinophils may be present if the microfilariae have been dead for some time. In each case the author in the original used the word *macrofilariae* and the statements refer as would be expected from the context to the adult worms.

Reports on the after-histories of patients who have undergone amputation of a limb for elephantiasis are scarce. RAO (p. 56) describes a patient whose leg was removed for elephantiasis and recurrent lymphangitis but the condition appeared in the other leg and in the stump. The amputation, therefore, conferred no benefit beyond the removal of elephantoid tissue.

BOZICEVICH and HUTTER (p. 1055) have used an extract of *Dirofilaria immitis* as antigen in skin tests for infection with *W. bancrofti*. All the subjects tested, who had been exposed to infection, gave positive results to the intradermal test at a dilution of 1 in 8 000 but some of these were positive to other antigens at the same dilutions. Complement fixation tests were not found to be useful. The authors conclude that the antigen, in a dilution of 1 in 8 000 may be useful in the diagnosis of filariasis provided that it is used with controls of canine serum and *Trichinella* antigen in the same dilution. Stronger solutions are less specific. The reactions produced may be immediate or delayed—the latter occur only in persons who give the immediate reaction.

CULBERTSON and ROSE (p. 772) have achieved some apparently favourable results in the treatment of cotton rats infected with the filaria *Leiomosoides curvius* by the use of stibamine gluconate (Neostam) in relatively large doses. They suggest that this drug may be useful in human filariasis.

CULBERTSON *et al.* (p. 770) report work on an antigen from *Leiomosoides curvius* of the cotton rat, which they used for intradermal tests in persons infected with *Loa* and *Onchocerca*. These appear to be favourable but more work is to be done on possible cross reactions. The same authors (p. 771) used antigens from this worm in skin tests, precipitin and complement fixation tests in a group of United States soldiers suffering from lymphadenitis and other signs of suspected filariasis. The tests gave 81–75 per cent. of positive results, but the correlation between them was only fair. It is probable that a significant proportion of persons not infected with filariae give positive results to these tests, and there may be difficulty in relation to infestations with *Trichinella*, *Ancyrostrongylus*, *Trichuris* and hookworms.

MEYER *et al.* (p. 770) have studied the development of the filaria of the lizard, which resembles *Onchocerca bancrofti* and discuss their findings in relation to the latter.

SCOTT (p. 683) describes what he believes to be the first case of onchocerciasis in a Gambian. *O. volutus* embryos were found in the anterior chamber of the eye and in the skin. In a second case there was oedema of the eyelid, ciliary ash and optic neuritis but no microfilariae could be found in the eye, though they are present in the skin. The author considers the possible causes of such a syndrome and concludes that the most likely explanation is the existence of raphialexia to the toxins of *O. volutus*. NETTEL (p. 305) discusses the routes of invasion of the eye in onchocerciasis and gives a classification of the lesions found throughout the body in an area of high endemicity in Mexico. Details could be sought in the original abstract.

LOEWENTHAL (p. 305) produces evidence to show that the papular dermatoses which may accompany onchocerciasis is not as has been thought due to the bites of *Simulium damnosum*. It is more likely that the skin is sensitized to a protein of the larvae of the worms and that the itching is due to this.

MAZZOTTI and OSORIO (p. 957) have experimented with two antigens prepared from *Onchocerca cercarientis* injected intradermally in onchocerciasis. Positive results are given in most diagnosed cases but there is a high proportion of false positives given by uninfected persons. The test therefore does not seem to be useful in diagnosis. WRIGHT and MURDOCK (p. 1054) have used an antigen prepared from *Dirofilaria immitis* in an intradermal test for onchocerciasis. All the subjects in whom *Onchocerca* embryos were found were positive to this test, but many of the controls (who were infected with other nematodes) also

gave positive reactions and the authors conclude that care is needed in the evaluation of intradermal tests

Enterobius Infection

YOUNG (p 141) found that 42 and 55 per cent of two groups of London children were positive for eggs of *Enterobius* on examination (repeated twice or thrice) by the 'Cellophane' swab technique. In the first group only 5 per cent showed eggs in the stools. DONALDSON (p 141) reports infestation with *Enterobius* in 46 and 31 per cent. of boys and girls in an institution in Ohio in which the living conditions were good.

JONES and HOLLANDER (p 596) show that radiations which are quite intense in sunlight are lethal to the eggs of *E. vermicularis* and *A. lumbricoides*. Sunlight itself is probably more lethal than the radiation produced by a mercury lamp especially if correlated with high temperature and low humidity

Trichiniasis

In a description of an outbreak of trichiniasis near Montevideo CLAVEAUX *et al* (p 501) make special note of a common condition in which there were transitory pulmonary symptoms and eosinophilia resembling Löffler's syndrome the authors therefore suggest that such findings should indicate a search for *Trichinella*. Similarly they think that in a patient with positive Wassermann or Kahn test but without history of syphilis trichiniasis should be suspected.

On the supposition that the toxic effects of infestation with *Trichinella* may be due to release of histamine through tissue destruction HAMANN (p 415) estimated the histamine content of blood and of various organs of satisfactorily infected guineapigs and rats. The results indicated some increase apparently due to the infection as against the values found in controls in the blood and in inflamed duodenal tissues but not in liver kidneys and skeletal muscles. There was no consistent correlation between blood histamine and eosinophilia. The results however were difficult to evaluate because there was great variability in both the experimental animals and the controls.

CARRICK (p 685) has investigated the effect of infestation with *Trichinella* in animals on the activity of the parathyroid glands. Details should be sought in the original abstract.

MAZZOTTI and PASTRANA (p 958) have found that calcified cysts of *Trichinella spiralis* tend to become disintegrated during the process of digestion with artificial gastric juice. This probably explains why the numbers of cysts revealed by this process is often smaller than the number found by the compression technique.

WRIGHT and OLIVER GONZÁLEZ (p 225) have examined by electrophoretic methods the sera of rabbits infested with *Trichinella spiralis* and have found an increase in gamma globulin. Antibodies against both larvae and adults were present in the gamma globulin. The authors recall that anti adult substances in serum protect to some extent against the intestinal stage of infestation but that the antilarval substances give no protection against intestinal infestation.

As a result of infestation of guineapigs with larvae of *Trichinella* of one sex only (so that there can be no multiplication) ROTH (p 59) has shown that a considerable degree of immunity against subsequent infestation by larvae of both sexes (as in natural infection) is induced. This immunity is therefore conferred by the intestinal phase of *Trichinella* and is apparently a true acquired immunity. It would probably be much more effective if larvae were present in blood and muscle of the host animal.

MELCHER (p. 225) has investigated the antigenic power of six chemical fractions obtained from larvae of *Trichinella spiralis*. Of these, the polysaccharide and the acid-soluble protein are the potent precipitating antigens and skin reactions are given with the acid-soluble protein, and an alkaline extract which itself is an earlier stage of the acid-soluble fraction. The results indicate that the acid-soluble protein is the fraction which other workers using a less refined technique have regarded as valuable for the diagnosis of trichinosis. There is no evidence of an antigen common to *Trichinella* larvae and adult *Ascaris* as has been claimed by other workers.

Some German medical officers have thought that treatment of trichinosis with Fouadin leads to improvement in the general condition though others are sceptical. SCHREIBER (p. 686) has failed to find any influence of Fouadin and other antimonials in affecting the infestation of animals with *Trichinella*.

Syngamus Infection

FOXT (p. 302) draws attention to three patients from whom *Syngamus laryngeus* (male and female together in copula) were removed from the oesopharynx or larynx. These slender worms which may be mistaken for dilated capillaries, cause constant irritation, with violent coughing. Removal cures the condition.

Charles Wilcocks

RABIES

A REVIEW OF RECENT ARTICLES XLIII *

L. VIRUS

JONESCU¹ states that he has failed to find in the literature any reference to studies on the autolysis of rabies-infected brain. He has therefore placed on record some observations on the subject. Within limits autolysis proceeds more rapidly the higher the temperature. The conservation of the tissue at very low temperatures and the associated prolonged survival of the virus is not due alone to the arrest or diminution of bacterial multiplication but also to the hindrance to the normal autolytic process. At 10°C. the advance of autolysis is difficult and at 18°C. relatively slow but it is favoured by raising the temperature to 37°C. At 50°C. autolysis is stopped completely.

The author has made observations at 18°C. and 37°C. The brains of a rabies-infected dog (street virus) and a normal or uninfected dog were removed aseptically and kept at 18°C. in separate glass containers under conditions in which bacterial contamination was excluded. The rabies-infected brain resisted autolysis for a longer time than the brain of the normal dog. After eight days the virus-infected brain appeared unaltered whereas the normal brain was flattened and there was a reddish exudate and this difference is attributed by the author to the inhibition of the normal autolytic enzymes by the virus.

Fragments were removed at intervals from various parts including the centre of the virus-infected brain, and these were emulsified and inoculated intra-cerebrally into rabbits in doses of 0.2 cc. After three months this brain was "completely autolysed" and it had assumed the appearance of a whitish paste. On microscopic examination the cells were found to be "completely killed."

¹For the forty-second of this series see this Bulletin 1945 v. 4, p. 165.

²Jo. escu D. Untersuchungen über die Autolyse von Tollwutgehirnen. Zeit. f. Bakt. I. Abt. Orig. 1945 Dec. 11 v. 151 No. 1 21-6 1 fig. [15 refs.]

and rabbits could no longer be infected by Intracerebral inoculations with suspensions of the brain but Negri bodies could be seen fairly well stained by the Lentz method.

In another experiment a reinforced virus J was used with an incubation period of three days and the presence of virus in the autolysed brain was demonstrated after four months by the inoculation of rabbits Intracerebrally. The incubation period in these was prolonged to six days. After four and a half months the virus was inactive. In a third experiment at 18°C. in which the

Babes fixed virus was used, active virus was demonstrable in the autolysed brain after three months.

Advantage was then taken of the increased rate of autolysis at 37°C to make more detailed observations than were possible at 18°C. After 24 hours at the higher temperature there were already macroscopic changes detectable in the rabies brains. There was a rose-coloured exudate which later became dark brown. After three days autolysis at 37°C a fragment from the brain was easily emulsified and after five days whitish formations appeared on the surface of the dark-coloured brain which had spread out on the bottom of the container. These efflorescences seemed to consist of crystals.

In an experiment at 37°C in which a rabbit fixed virus was employed observations were made on an autolysed rabies brain (rabbit) and an autolysed normal rabbit brain. In a period covering 15 days the pH of both brains altered from 7.8 to 7. Virus was detectable by the inoculation of white mice after nine days but not after 11 days or longer. Similar results were obtained in experiments with the brains of a dog and two cattle infected with a street strain of virus. Microscopic studies were made on the autolysed brains of rabbits and dogs infected with fixed strains of rabies virus and on the autolysed brains of a dog and cattle infected with a street strain. After periods of 2 4 6 8 10 and 13 days at 37°C portions of the Ammon's horn of these brains were removed and fixed in acetone embedded in paraffin and sections were stained by the Lentz method.

After three days autolysis fine oxyphilic granules were observed in the Ammon's horn of the brains of the animals infected with the fixed strains of virus. Some were like small Negri bodies and they were not found in the autolysed brain of a normal animal.

The microscopic findings in the sections of the Ammon's horn of the autolysed brains of the animals infected with street virus were as follows. —After one day at 37°C the cytoplasm of the cells had disappeared the nuclei showed first pyknosis then achromatosis and finally chromatolysis. Whereas the nuclei after 10 days had completely disappeared the Negri bodies especially the mature forms with internal structure as well as the morula forms or forms with basophilic inclusions maintained their characteristic appearances and were distinctly oxyphilic. Up to the ninth day virus could still be demonstrated in the autolysed rabies brains by the inoculation of rabbits by the intracerebral route. After that time although Negri bodies were still present active virus could not be detected. The Negri bodies in the autolysed brains appeared to be double the size of those seen in the non-autolysed tissue. [The certainty with which it can be determined that the brain tissue is infective or non-infective is controlled by the limitations of the sensitivity of the test employed to decide this. Any attempt to correlate virus infectivity with the presence or absence of oxyphil granules or Negri bodies must be considered as purely speculative. It might be interesting to consider these observations in relation to the theory of REMLINGER and BAILLY on the attenuation of the virus of rabies during the preparation of vaccine by the Pasteur method (see this *Bulletin* 1943 v 40 195 1944 v 41 904)]

ii. Symptoms and Diagnosis

BREAULT² refers to a human case of rabies which occurred during a localized outbreak in the summer and autumn months of 1944 in which many dogs and cats and a cow contracted the disease. The case is chiefly of interest because of the history and the dog which bit the boy did not appear to be rabid or "wild." It bit the boy in the leg on provocation, and disappeared. The wound was deep and lacerated and was stitched. The stitches were removed one week later and the wound healed normally. The boy was well for seven weeks. On August 22 he complained of crampy pains in the leg, and was feverish. On August 25 because he still had fever and had backaches and stiffness of the dorsal muscles he was sent to hospital, as poliomyelitis was suspected. He was, however, sent home the same day as this disease was ruled out. Three days later he had delirium and hydrophobia and he was readmitted to hospital on August 29. There was unbearable itching of the leg which had been bitten. The boy died four days later and Negri bodies were demonstrated in sections of the hippocampus and cerebellum removed at autopsy.

HERZOG³ states that he found independently in 1941 a method for the diagnosis of rabies which had been "described by VAN GEHUCHTEN and VELLS in 1900 but had been completely forgotten after the discovery of Negri bodies. [Observations on the limitations of the method were made by the reviewer when discussing a previous paper by the author on the same subject (this *Bulletin*, 1943 v 40 199)] it was indicated that the observations of van Gehuchten and Vells had not been completely forgotten. As already pointed out, the presence of nerve ganglionic lesions may be said to provide strong presumptive evidence of rabies if the history suggests it, and this should be confirmed by inoculation of animals if possible with such suitable material as may be available. It was realized early that even greater prudence would have to be exercised in interpreting negative findings in the histological examinations of nerve ganglia from suspected cases (in a book published in 1903 the year Negri bodies were first described, viz. *Les Maladies Microbiennes des Animaux* by NOCARD and LECLANCHÉ, v 2, p 453-5 reference is made to the lesions first described by van Gehuchten and Vells.)

In the present paper the author reports that of 75 subjects (7 human beings and 68 animals) suspected of having rabies, 52 were found to have the disease.

A comparison was made of different methods of diagnosis by microscopic examination of nervous tissue such as examination for Negri bodies in the Ammon's horn, histological examination of the *ganglion nodosum* of the vagus nerve, the superior cervical sympathetic ganglion or the mesencephalon and the medulla. Incidentally in the literature on rabies one sees quite often a statement to the effect that no Negri bodies were found in the *Cornu Ammonis*, but the fact should not be forgotten that although Negri bodies are often found in the hippocampus even when the disease is fully developed they may be absent from this site and from the cerebellum, but may be found in other parts of the brain in so-called predilection sites (see for example this *Bulletin* 1935 v 32, 173 and 174 for observations by MURATOWA, THOMAS and JACKSON and NICOLAU and KORCOWSKA). In "almost 50 per cent." of Herzog's 52 cases of rabies "he could not find Negri bodies in sections of the *Cornu Ammonis* stained by the Lentz method. However simultaneous histological examination of the *ganglion nodosum* from the same cases always disclosed the

²BREAULT H. J. *Hydrophobia. Canadian J. Comp. Med.* Gardemais, Quebec. 1945 Apr. 9 No 4 110-15.

³HERZOG, E. *Histologic Diagnosis of Rabies Arch. Pathology* 1945 Apr. 39 No 4 278-60 2 figs.

alterations described by van Gehuchten and Nels in 1900 and again described by the present author. It is suggested that if examination of the Ammon's Horn and ganglion nodosum yields negative results the lesions of a rabies encephalitis may be sought in the mesencephalon and medulla. The author states that if the results of such examinations are all negative it is not worth while to inoculate test animals as the bitten person may be considered free from rabies and spared vaccination but in doubtful cases white mice should be inoculated and a result will be yielded in 15 days.

iii. Pathology

JONESCU⁴ refers to three cases of natural immunity two in dogs and one in a male goat. He previously recorded two similar cases in dogs (this Bulletin 1935 v 32 609 1936 v 33 p 747)

He points out that individual differences in susceptibility to various infective agents are exhibited by animals which can be infected with these agents. In the case of rabies there are known to be species refractory to infection, cold blooded animals snakes and fish partially refractory species such as hibernating animals and susceptible species such as dogs cats rabbits etc. In rare cases certain animals belonging to the susceptible group may exhibit a high spontaneous degree of resistance to inoculation with virus but this resistance can often be broken down on reinoculation by more massive doses of virus especially by the intracerebral route. In one of the two previously recorded instances the dog after resisting an intraocular inoculation of a reinforced virus strain J received in succession nine intracerebral inoculations of 1 cc of a 1/50 dilution of a fixed strain of virus. The author concluded that the dog had a natural immunity.

The cases recorded here were in domestic sheep dogs and a goat.
Case 1 — In December 1940 nine dogs were inoculated with 0.5 cc. of a 1/20 suspension of a fixed strain (dog) of virus intracerebrally. One 3-year-old sheep-dog withstood the inoculation. In January along with four other dogs it received a second intracerebral inoculation of 1 cc. of a similar suspension. It resisted this whereas the four other dogs did not. However the dog succumbed to a third inoculation made in January 1943 and its brain proved infective for a rabbit by intracerebral inoculation. The period of paralysis was more prolonged in the resistant as compared with the control dog eight days instead of two days.

Case 2 — On August 21 1941 20 dogs were inoculated intracerebrally with 0.5 cc. of a 1/20 suspension of fixed virus. 19 developed the disease on the seventh day but one three year old sheep-dog resisted. It received a second intracerebral inoculation of 1 cc. of a similar suspension on August 30 1941 along with 15 other dogs. It resisted whereas the 15 dogs developed paralysis on the seventh day. No symptoms developed after a third intracerebral inoculation of 1 cc. of a 1/10 suspension of fixed virus on May 17 1943. Four control dogs showed paralysis on the seventh day. The dog succumbed, however to a fourth intracerebral inoculation on June 24 1943. The paralysis lasted 13 days as against the usual two days. Two rabbits inoculated intracerebrally with a suspension of its brain remained healthy suggesting that autosterilization had occurred.

The history of the goat is somewhat similar. It resisted three intracerebral inoculations with fixed virus but finally developed paresis which lasted 58 days after the last inoculation and it died and virus was recovered from its brain by inoculation of rabbits intracerebrally. Studies were made of blood samples

⁴JONESCU D. Untersuchungen über die natürliche Immunität bei der Tollwut. Zeit. f. Bak. I. Abt. Orig. 1944 May 10 v 151 No 4/5 254-60 [18 refs.]

collected from the two dogs five days after each inoculation. An increase in the number of eosinophils in the blood was observed up to and after the time when the fatal inoculations were given. The author has restated his opinion, expressed in 1935 [reference above] that the eosinophilia can be used as an indication of the degree of immunity and suggests further that it might be used as a guide to the issue in following the course of vaccine treatment. He also describes experiments *in vivo* and *in vitro* in support of his contention that the leucocytes probably played a considerable part in the destruction of the virus introduced, and the resistance of the animals under discussion, but his results and conclusions are not entirely convincing. He could not demonstrate that the blood serum collected from either of the dogs at different times during the course of the experiments had any neutralizing action on the virus (the tests were not made in such a way (*i.e.* not on a quantitative basis) that much reliance could be placed on the author's negative findings). The author believes that other factors, such as a basic hereditary resistance cannot be excluded from the discussion of such observed cases of exceptional resistance to infection [there are of course other possibilities in a country in which the disease is endemic: for instance 1. a previous light infection of the animal by a peripheral route such as might result from a bite 2. intra-uterine infection with virus with a non-fatal issue at birth 3. congenital as distinct from hereditary immunity].

iv *Methods of Treatment and Statistics.*

DURIZOT³ reports that the strain of fixed virus used for vaccine production at Dakar is the Tangiers strain sent in 1922 and at the time of writing it had been passaged 416 times at Dakar and 944 times since its receipt at Tangiers. The incubation period in rabbits inoculated intracerebrally is 5 to 6 days. A carbolyzed vaccine of the Ferra type is employed and sheep are inoculated with the rabbit virus for its preparation but the strain is never passaged from sheep to sheep incidentally—it is understood that owing to the shortage of rabbits sheep are now used also at the Pasteur Institute Paris for vaccine production]. A 5 per cent. suspension of nervous substance is used and carbolic acid is added to produce a concentration of 1 per cent. The vaccine is distributed in 6 cc. amounts in ampoules and two bacterial sterility tests are carried out anaerobically and aerobically the first when the brain is removed from the sheep and the second when the vaccine is put into the ampoules. The vaccine for use at the central institute is placed at 25°C. for 24 hours and then stored at 5°C. If the vaccine is for use elsewhere in the service it has to be transported by aeroplane and is therefore not first placed at 25°C. before despatch—it is placed in cold store on arrival at the subsidiary centre. If sent out again it is kept in ice during transit. The vaccine is considered to be usable up to four months after preparation if used at the central institute and up to two-and-a-half months if distributed to sub-stations or centres of medical assistance. During 1941 and 1942 409 patients were treated in the whole territory of the A.O.F. and no deaths and no paralytic or other accidents were recorded.

v *Rabies in Animals*

HUDSON⁴ reports that rabies has been known for a long time to the native inhabitants of the South Kavirondo province of Kenya. They call the disease

³AFRIQUE OCCIDENTALE FRANÇAISE. RAPPORT SUR LE FONCTIONNEMENT TECHNIQUE DE L'INSTITUT PASTEUR EN 1942. DUBREUX C.] pp. 41-8. Service de la rage.

⁴HUDSON J. R. A Short Note on the History of Rabies in Kenya. *East African Med. J.* 1944 Nov. v. 21 No. 11 323-7. [10 refs.]

in dogs and jackals swao. The author believes that the disease must have occurred in the colony before the advent of Europeans. STORDY in 1909 however stated in the Annual Rept. of the Veterinary Department that no case of rabies had been recorded in East Africa and this statement appeared again in the 1912-13 report. The earliest case to be recorded occurred near Nairobi in October 1912 and was that of a dog which had been attacked and bitten by a jackal. Negri bodies were found in its brain and confirmation of the diagnosis was obtained by experimental animal inoculations. Further cases all with the same history followed rapidly in the Nairobi and Kiambu areas. Jackals were reported to have lost their fear of man and to have attacked natives without provocation. The outbreak lasted till 1918. Rabbits were infected by inoculation with material collected from the infected animals.

The first human case appears to be that recorded by GREEN in 1928 [this *Bulletin* 1928 v 25 709]. A native woman living in Central Kavirondo died from rabies a month after having been bitten by a dog. It has been stated that the disease was more or less enzootic in the North Frontier Provinces between 1912 and 1929. The next case reported was in 1931 and the disease persisted in certain parts until 1936 and in others to 1938. A new wave of rabies started in 1944. The disease appears to be conveyed in the forest areas and has not spread down into the Rift Valley. Rabies in East Africa appears to be spread by jackal and dogs and there is no evidence to date of *Lysseridae* playing any part as in South Africa.

It has been found that jackals which attack human beings or enter houses or compounds are infected with rabies on examination. The dumb or paralytic form is probably more frequent than the furious type. In the majority of cases the disease could be transmitted to mice and rabbits by intracerebral inoculation and Negri bodies could be demonstrated. In four cases out of the total of 167 recorded Negri bodies could not be demonstrated in the hippocampus of the infected animals and the diagnosis was confirmed by passage to rabbits and mice.

Apparently the natives know rabies as a disease of dogs and do not attach any importance to the bite of the infected animals. Human cases are attributed to witchcraft or the casting of spells. A similar position exists in French African Territory where the natives call the disease in dogs *oulou fato* [it seems that the Kenya strains of rabies virus are not like the *oulou fato* strain studied by NICOLAU MATHIS and CONSTANTINESCO (this *Bulletin* 1934 v 31 145) associated with blue Negri bodies—staining blue with Mann's double stain].

VI. Miscellaneous

REMLINGER⁷ stresses again the necessity of a Second International Conference on Rabies. He now suggests that the meeting place should be in Europe and proposes Spain as a likely spot with many points to recommend it. He urges that the representatives of the different countries should be those actually engaged in the study of the disease and that informality should characterize the discussions. The author tentatively sets out a number of matters which require urgent attention. The list is roughly as follows with certain trimmings by the reviewer. (1) The advisability and practicability of standardizing rabies vaccines giving due consideration to the strain or virus to be used the method of preparation and the technique and standard to be aimed at in estimating potency. (2) Discussion of new information on immunological and immunogenic differences between strains of the virus of rabies and of the factors which may

⁷REMLINGER P. Sur la nécessité d'une nouvelle conférence internationale de la rage Arch Inst Pasteur d'Algérie 1944 June, v 23 No 2 141-4

affect the characteristics of a strain. (3) Discussion of the possibility of vaccinating domestic animals, including dogs cats horses, sheep cattle goats and pigs and of the arguments for and against the general application of such a policy in countries in which the disease is endemic. (4) Consideration of the experimental animals of choice for different purposes diagnosis, determining virus potency the antigenic potency of vaccines—mouse rabbit guinea pig dog monkey?

Rabies is a world-wide problem and there should be the maximum exchange of information on the disease and on the methods employed in the different countries to combat and control it. Some countries are more favourably placed geographically than others, and in them it is easier to prevent the introduction of the disease and to limit its spread and the possibility of its becoming endemic, should the regulations in force break down. The British Isles among other countries is so placed but while such a country may be regarded with envy by its less fortunate neighbours, that is no reason why its endeavours should not be fully comprehended and, if at all possible imitated to some degree. Co-operation is necessary between nations in stamping out or limiting the ravages of such a dread disease. In the same way our own Dominions and Colonies from which danger may spring should have knowledge of the possible loopholes in the system of control. Recently attention has been drawn in a *Monthly Bulletin*¹ published under the aegis of the Medical Research Council and in an Annotation in the *Lancet*² to the risk of the reintroduction of rabies into Great Britain if due attention is not paid to the regulations which are in force. In view of this risk it is imperative that everyone should have full knowledge of the possible effects of criminal negligence in evading the regulations. As Fyfe³ has pointed out in describing a case of rabies in man, many people (and this includes medical and veterinary officers in Great Britain where outside quarantine kennels no case of rabies has been confirmed since 1922) have forgotten the serious nature of the disease and are not fully aware of the means by which the country has been kept free of it. 'It may be recorded here that, from information received from the Ministry of Agriculture there were 2,557 cases of rabies in animals from the year 1887 to 1898 a period of 11 years. Regulations which since 1897 have gradually made more stringent the restrictions on the importation of canine and feline animals, have produced a most satisfactory result. There were 48 cases between 1897 and 1902 (six years) but between 1903 and 1917 there were none. During the latter half of the 19th century the annual human deaths from hydrophobia increased to the alarming total of 79 in 1877. Since 1888 only two deaths from hydrophobia have been recorded. The regulations in force require all canines and felines landed in Great Britain from abroad to be quarantined for a period of six calendar months after landing on premises approved by the Ministry of Agriculture. Now some may imagine that such a rule is over-cautious, and perhaps unnecessary. In order to stifle such an objection it should be pointed out that, from information received from the Ministry of Agriculture there have been no less than 16 cases of rabies in quarantined dogs from 1919 to 1939 a period of 21 years. In six of these cases the disease developed from 1 to 12 days after the dog was landed in this country, in five the disease developed between 1 month and 3½ months after the dog was landed and in four cases, between 4 and 5½ months. In the 16th case the period of quarantine was up on November 1st, 1929 and the dog was kept in isolation for a further period at the

¹MONTHLY BULL. MINISTRY OF HEALTH & EMERGENCY PUB. HEALTH LAB SERVICE (DIRECTED BY MED RES COUNCIL) 1944 Dec. v 3 220-22. Rabies.

²LANCET 1944 Nov 11 623-9 The Menace of Rabies.

³FYFE J G Case of Rabies in Man. *Lancet* 1945 Jan. 13 53-4.

owner's request it developed rabies 6 months and 24 days after arriving in Britain.

The experience of the Ministry of Agriculture has therefore fully justified the six months quarantine period. The period of six months quarantine is based upon the period of incubation of rabies which may be longer even than six months but the cases in which the incubation period exceeds six months are very exceptional. It is not considered practicable to legislate for these exceptional cases but of course it is realized that there is still a risk as the above records show there are however other regulations for dealing with rabies in Great Britain including notification of suspected cases muzzling orders etc. The disease was reintroduced into this country once only since 1917. This was after the armistice in 1918 and was due to a dog or dogs illegally imported by a demobilized soldier and by others. The consequences were very serious. From 1918 to 1922 there were no less than 325 cases of rabies in animals and there were nearly a thousand suspected cases reported. 358 persons were bitten 123 of these by dogs known to be rabid and 144 persons received vaccine treatment.

The conditions which in 1918 facilitated the illegal importation of dogs and other animals have returned in an aggravated form and it would be rash to assume that the present sequence of 23 years freedom from rabies (apart from cases in imported dogs in quarantine) will continue unbroken.

It would appear that attention should be drawn on a larger scale to the risks of serious consequences attendant on the criminal evasion of the importation regulations.

In this connexion it is of interest that on the 4th July 1945 an Order was issued by the Ministry of Agriculture entitled the Importation of Dogs and Cats (Amendment) Order of 1945. This Order allows the importation of dogs under a licence granted by a commissioned officer of His Majesty's Army authorized in that behalf by an assistant Under Secretary of State at the War Office in the case of a dog owned by a member of H.M. Navy Army or Air Force. Such dogs shall be detained and isolated for a period of six calendar months after landing in Great Britain upon premises which have been approved for the purpose of such detention and isolation by or on behalf of the Secretary of State for War and which are under the control of the Royal Army Veterinary Corps.

There will therefore be in future two forms of licence under which dogs may be imported into Great Britain viz. —

(1) That issued by Authorized Army Officers in respect of dogs to which the special scheme applies. These dogs will be detained in the specially provided quarantine kennels.

(2) That issued by the Ministry of Agriculture and Fisheries in respect of any other dogs and cats. These animals will as hitherto be detained in approved quarantine kennels under civilian control.

It will be open to members of the services who do not wish to or who cannot take advantage of the special service scheme to make use of those facilities which are available to members of the general public in all such cases the necessary licences must as hitherto be obtained from the Ministry of Agriculture.

In a circular letter sent to all local authorities for the purposes of the Diseases of Animals Acts and to all Chief Constables the Ministry explains the implications of the Order which has been referred to above and urges that when particulars of the scheme are published warnings should be given to members of H.M. Navy Army and Air Force about the dangers of rabies and of the risks attendant upon the smuggling of dogs or cats into Britain.]

In the *Bulletin*⁸ referred to above information is given on the methods employed in Great Britain for dealing with rabies should cases arise, and the addresses are given of centres from which vaccine for anti rabies treatment of

human subjects may be procured, and the address to which material collected from suspected cases should be sent for diagnosis. [The reviewer would like to see the more general use of the mouse for more rapid biological diagnostic tests (see this *Bulletin* 1937 v 34 677 1943 v 40 652-4) and considers it to be advisable also for vaccines which are intended for anti-rabies treatment to be submitted to potency tests (this *Bulletin* 1941 v 38, p. 161). Periodic examination of the characteristics of the fixed strain of virus used for the preparation of the vaccine should also be made. He would also like to suggest the adoption of a better method of sending the material, head and neck or brain and cord, for diagnosis so as to avoid the putrefaction and liquefaction of the nervous tissue to be examined, which so often occurs.]

In the annotation in the *Lancet* referred to above reference is made to the local treatment of the bites of rabid animals. [It should be pointed out that the sucking of the bite with a view to removing infected saliva as recommended would be a dangerous procedure as it is generally accepted that, on a mucous surface such as the mouth, or where the skin is definitely broken, infection with rabies can occur. There is some evidence also that thorough syringing with a 20 per cent. green soap solution would be as effective as the more drastic method of cauterization (see this *Bulletin* 1944 v 41 173-5 180 and 912) and with regard to the question of WEBSTER'S remarks on an anti-rabies vaccine treatment referred to in the same annotation, they have been commented on by the reviewer (this *Bulletin* 1943 v 40 269-70 656 and 1944 v 41 180) with regard to statistical evidence on anti-rabies vaccine treatment in human beings. Webster's scepticism arose from the unsatisfactory results obtained in potency tests on many commercial vaccines in America. He was also justifiably critical of much of the evidence produced in support of the effectiveness of anti-rabies vaccination. Nevertheless what he was striving for was the development of methods of estimating the potency of vaccines and standardization of the biological product. Yet his critical attitude and scepticism would not justify the withholding of vaccine treatment and indeed be said "persons exposed to rabies should be given treatment with confidence that there is small likelihood of development of the disease. What he implied in his attitude of scepticism was that if anti-rabies treatment was to be applied, the vaccine should be tested in some way for antigenic potency so that the method of treatment should not be condemned because of the use of an inferior product. Webster's attitude is in the reviewer's opinion, not always correctly interpreted. It would perhaps be opportune to state here that it is felt that it would be extremely useful if there was a centre in Britain for the study of rabies. There are many problems which could be tackled, such as the study of the immunogenic, immunological and other properties of fixed strains of rabies virus and the methods of estimating the potency of vaccines. Further information is also required on suggested type immunological differences between strains of street rabies virus and on the nature of the virus and its physico-chemical properties. Such a centre might well work under the aegis of the Medical Research Council and the Agricultural Research Council, and the knowledge which was acquired would be useful also to the Colonial Office and the Ministries of Health and Agriculture. Surely it would be useful also that there should be an instructional centre for medical and veterinary officers proceeding overseas on such an important disease as rabies. It would not be difficult to organize and run such a unit.]

Aujeszky's Disease

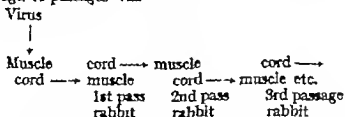
HIRT¹¹ records that in his experience swine, inoculated intracerebrally with the virus of Aujeszky's disease contained in a suspension of brain, nearly always

¹¹HIRT G. Infektions- und Immunversuche mit dem Virus des Aujeszky'schen Krankheits. *Arch. exp. appl. Pathol.* 1942, 78 186-90

succumbed to the infection death ensued in 1 to 2 days after the first symptoms were observed. The incubation period was usually 3 to 4 days but was occasionally as long as 6 days. There was a sharp but transient rise of temperature 12 to 24 hours before the onset of symptoms. At autopsy gastro-enteritis and oedema of the lungs were sometimes seen but at other times there were no macroscopic changes. There were some infiltrative lesions in the c.n.s. The virus could be recovered from the blood spleen and the lung.

Two pigs were inoculated intracerebrally with virus and at the same time they received 50 cc. of an immune serum one intravenously and the other subcutaneously. The potency of the serum was such that 0.01 cc. neutralized 25 rabbit fatal doses of virus and it was estimated that the 50 cc. dose of serum should have been capable of neutralizing 125 000 rabbit doses of virus. Both pigs died after an incubation period of 6 days and they died on the seventh and eighth day respectively. Two pigs which had been inoculated many times with virus-infective rabbit brain and two pigs which had recovered from a spontaneous attack of the disease were shown to have immune bodies in their sera and when inoculated intracerebrally with virus all four animals survived.

HIER¹² in a second paper states that 0.1 cc. of a 1 per cent. suspension of virus infected brain material almost always leads to a fatal inoculation. Eight passages of virus were made intracerebrally in swine and the author records that there was no alteration in the symptoms the incubation period or duration of the disease. On three occasions during the course of the eight passages two swine were inoculated *viz.* at the fourth fifth and seventh passages. On two occasions *viz.* at the fourth and fifth passages one pig died and one survived and the sera of the surviving swine were shown to be capable of neutralizing the virus of Anjeszky's disease. In rabbits 50 successful passages were made intracerebrally. In another series of passages in rabbits suspensions of the lumbar cords inoculated into the thigh muscles were passaged successfully in series through 40 passages *viz.* —



In a third series of passages in rabbits suspensions of the brains of rabbits inoculated into the thigh muscles were passaged in series in the same way but the rabbits survived after the second or third passages.

In other experiments virus was inoculated into the shoulder muscles of 14 rabbits. All the rabbits developed typical symptoms and died. In all the 14 rabbits virus in sufficient amount to infect rabbits when inoculated intramuscularly was demonstrable in the cervical cords but in only six cases in the brain and in three cases in the lumbar cord. Rabbits were also inoculated intracerebrally with suspensions of the rabbit brains of which suspensions had failed to infect when inoculated intramuscularly and negative results were recorded.

[The information contained in the above two papers by HIER on Anjeszky's disease confirms and extends what is already known about its pathology to the knowledge of which he has already made valuable contributions—see pages 756 758 and 759 of a review by GALLOWAY (this *Bulletin* 1939 v 36 195)]

Ian A Galloway

¹²HIER G. Bei der Anjeszky'schen Krankheit ist der Virusgehalt des Zentralnervensystems durch die Infektionsstelle bedingt. *Arch. wiss. prakt. Tierheilk.* 1942, v 78 191-4

MALARIA.

RUSTOMJEE K. J. Observations upon the Epidemiology of Malaria in Ceylon. *Ceylon Sessional Paper XXIV—1944* Dec. 32 pp. 5 maps 8 diagrams & 4 charts. Colombo Ceylon Govt. Press. [Price 2 50]

This lengthy report describes the distribution and intensity of malaria in Ceylon and gives a brief account of malaria epidemics in that island with detailed information regarding the incidence of the three species of malaria plasmodia during the epidemics of 1939 and 1943.

Variations in rainfall permit of the division of Ceylon into dry intermediate and wet zones. The incidence of malaria is high over nearly all the dry zone, except in the hilly areas above 3 000 feet but epidemics do not occur. Moderate to severe malaria characterizes the intermediate zone. In the wet zone malaria incidence is low but epidemics are liable to occur. Spleen rates were high over the whole island in 1936 as a result of the great epidemic of 1934-35 in the dry zone they remained high but elsewhere they reached normal levels after one or two years. Similar findings followed the 1939 epidemic. In the absence of epidemics *P. vivax* and *P. falciparum* are about equally prevalent in the wet zone. *P. falciparum* is more prevalent than *P. vivax* in the intermediate zone. In the dry zone *P. malariae* is pre-eminent. Death rates return to normal within two years of a major outbreak, infant mortality rates more quickly still.

Widespread epidemics have occurred at intervals of 4-6 years or slightly longer and are commonly confined to the wet and intermediate zones. Here the drying up of river beds consequent upon deficient rainfall, leaving pools favourable to the breeding of *A. culicifacies* favours epidemic prevalence. Excessive rainfall and floods may cause increased malaria incidence in the malarious dry zone but not elsewhere. The months of April to June and October to December are the seasons of most frequent epidemic manifestations in the wet and intermediate zones. The season of maximum malaria prevalence in the dry zone is October to February. No precise measurements of any of the numerous factors involved in the causation of epidemics have as yet furnished reliable data for forecasting such epidemics with any degree of reliability.

During the spring epidemics of 1939 and 1943 *P. vivax* was more prevalent than *P. falciparum* in the wet zone while the reverse was the case in the intermediate zone. *P. malariae* played no part in the epidemic manifestations in either zone.

A complete summary of the large amount of information contained in this report is not possible.

Norman White.

GEIGY R. Malaria in der Schweiz. [Malaria in Switzerland.] *Acta Tropica* Basle, 1945 v 2, No. 1 1-16 11 figs. [17 refs.]

According to GALLI VALERIO there were many foci of malaria in Switzerland in the first half of the 19th century and it is remarkable that, as in Sweden and Finland, some time between 1870 and 1890 one focus after another died out although the anopheline mosquitoes remained unchanged in numbers and distribution. This was not due to greater severity of climate during that period, but many sanitary works were carried out and more medical treatment was given. Other possible influences were the increase of cattle (resulting in the attraction of the mosquitoes away from man and tending to increase zoophily) and, as GALLI VALERIO suggested in 1901 the development of immunity on the part of the mosquitoes against *Plasmodium vivax*. The last question has

been investigated by the author at Basle where a group of interned persons suffering from benign tertian malaria acquired mostly in Sardinia were under medical care.

The chief anophelines to be considered were *A. maculipennis* var *typicus* and *A. bifurcatus*. A small station was established in Basle University in July 1944 and adult mosquitoes from several of the old malaria foci were obtained. Very little breeding out from eggs and larvae was done. Although the mosquitoes were kept in warm surroundings the hibernating state was evident by the end of October. All male and many female *A. maculipennis* die a few fertilized females with immature ovaries survive and no larvae can be found. All adult *A. bifurcatus* disappear but larvae from the latest deposited eggs reach stage 3 or 4 and survive the winter being found in frozen ponds and slowly flowing streams.

According to SAUTET [*Ann de Parasitol* 1933 v 11 161] the stage 4 larva of *A. bifurcatus* can be stimulated to develop into the imago by means of potassium permanganate or chlorinated water but experiments by the present author with this aim were completely unsuccessful all the larvae dying. When the larvae are simply kept at room temperature an occasional imago emerges but they are too few for practical use.

Mosquitoes caught chiefly in cattle houses fed at once on man showing no sign of possessing any firm zoophily. After feeding they were kept at 24°C. The results are shown in the following table —

Sporogony researches (3rd August to 8th December 1944)

	<i>A. maculipennis</i>	<i>A. bifurcatus</i>	Total
1 Mosquitoes used	69	113	182
2 Placed once on a gametocyte carrier (no infection)	27	15	42
3 Placed many times on a gametocyte carrier	42	98	140
4 Infected (8.6 per cent.)	6	6	12
5 Oocysts in stomach only	1	5	6
6 Infection of salivary glands only	2	—	2
7 Both stomach and glands	3	1	4

CIUCA *et al.* (*Acad Roumaine Bull Sect Sci* 1942 v 25 96) had previously found with *P. falciparum* and *A. maculipennis* var *aloparens* that repeated feeds produced a higher rate of infection than single feeds. In the present experiment the shortest time between feeding and finding cysts in the stomach wall was 10 days. It was often 20 or more days before the salivary glands became infected. In three cases the different ages of the cysts showed that superinfection had occurred. The infected mosquitoes were not used to reinfect man but the sporozoites were active and probably infective. One of the most heavily infected stomachs showed 400 cysts.

The stomachs and glands were examined in Ringer's solution and were fixed in Duboscq fluid, Carnoy fluid, or sublimate-alcohol-acetic acid mixture. Sections were stained with Heidenhain's haematoxylin.

The material was insufficient for a close cytological study. No difference was observed in the evolution of the cyst in the two species of mosquito. Mitosis

was not seen in the development from a uninuclear to a quadrinuclear cyst further development agreed with textbook descriptions.

The infection of the glands varies all three lobes may be swollen, or the diverticula may be very slightly expanded and difficult to distinguish from a normal gland.

The author discusses the epidemiology of malaria in Switzerland and gives various reasons for concluding that there is little chance of its again becoming prevalent.

The paper is illustrated by excellent photographs.

J F Corson

YOUNG M. D. Studies on the Periodicity of Induced *Plasmodium vivax*. J National Malaria Soc. Tallahassee, Fla. 1944 Dec. v 3 No 4 237-40

The assumption that paroxysms of *P. vivax* malaria have a periodicity of exactly 48 hours is not true for some strains of that parasite. The majority of the observations recorded in this paper were carried out on the St. Elizabeth strain of *P. vivax* which is used in the South Carolina State Hospital for the treatment of neurosyphilis. Patients exhibiting a tertian type of fever indicative of a single brood of parasites were selected. Measurements were made of the intervals between one fever peak and the next. The patients' temperatures were taken four-hourly hourly when over 100°F. The peak of the segmentation of the parasites precedes the peak of fever by several hours; the peak of fever coinciding closely with the peak of young ring forms. Of such observations 307 were made in patients who had been infected by injection of infected blood, and 94 in patients who had been infected by mosquito bite. There was no significant difference between the paroxysmal intervals in these two groups of patients. The average interval was 43.42 hours.

Twenty-five similar observations were made on two patients infected with a strain of *P. vivax* contracted in the New Hebrides. The average paroxysmal interval was 45.78 hours.

Sixty-four paroxysmal intervals in patients infected with a strain of *P. vivax* used for malaria therapy in Baltimore averaged 41.52 hours.

The results indicate that different strains may each have a characteristic periodicity which would be of value in distinguishing such strains.

Norman White

BIRD J. Malaria Eradication by breaking the Sporogonic Cycle of the *Plasmodium*. Preliminary Note. Bol. Asoc. Med. de Puerto Rico 1945, Feb. v 37 No. 2, 56-7

As the tissues of anopheline mosquitoes are the natural medium in which the sexual cycle of development of malarial parasites takes place, it occurred to the author that the injection into man of an antigen prepared from the mosquitoes might stimulate the formation of antibodies having the power of preventing the development of gametocytes. He ground up 1 gm. of anopheline mosquitoes in 100 cc. of distilled water and filtered through filter paper and then through a Berkefeld filter. A dose of 2-4 cc. of this filtrate repeated 2-3 times at 8-day intervals was injected intramuscularly into volunteers and patients with syphilis of the nervous system. They were afterwards infected with malaria by inoculation of blood containing asexuals. In some cases no gametocytes were found and in others only male gametocytes. The author therefore concluded that the sporogonic cycle had been broken by this means. [No details of the experiments are given in this preliminary note.]

J F Corson.

RUSSELL P F KNIFE F W RAMACHANDRA RAO T & PATNAM P Some Experiments on Flight Range of *Anopheles culicifacies* J Exper Zool Philadelphia Pa 1944 v 97 No 2 135-63 13 figs. [15 refs.] (Summary taken from Rev Applied Entom Ser B 1945 May v 33 Pt 5 71)

The following is based on the authors summary and conclusions Nine experiments on the flight range of *Anopheles culicifacies* Giles were carried out in Madras between 22nd July and 28th October 1941 Mosquitos marked with coloured dust were released at a point around which 80 call baited traps were arranged in concentric circles with radii of $\frac{1}{4}$, $\frac{1}{2}$, $\frac{3}{4}$ and 1 mile The larger circles had respectively two three and four times as many traps as the smallest so that the traps were the same distance apart on each circle Some 207,800 mosquitos were collected in the traps and in villages just beyond them and examined for evidence of coloured dust The greatest observed flight range was between 1.5 and 1.75 miles Nine mosquitos flew this distance in a night and seven others in two nights Three of the flights were against the wind

The object of the study was to find a basis on which to fix the limits of the zone in which anti mosquito measures are necessary for malaria control. The data obtained were analysed statistically If the flight-ranges of the mosquitos released had been random a similar proportion should have been taken on the periphery of each of the four zones of the experimental field. The observed dispersion never achieved this and it must be concluded that inhibiting factors prevented a random distribution of flight-ranges The relationship between mosquito captures (y) and distance proved to be hyperbolic with an equation of the form $y = a - x^b$ where x is the distance in miles from the point of release a is the number of mosquitos expected on the circle with radius of 1 mile and b is the measure of flight inhibiting factors The value of a is determined primarily by the number of mosquitos released The value of b is a measure of the extent to which the flight ranges of a specific group have been inhibited. Thus the b value for males of *A. culicifacies* (1.602) was greater than that for females (0.681) Mosquitos flying with the wind were less widely dispersed than those flying across or against the wind Mosquitos taken in nature flew greater distances than those bred in the laboratory although the difference between the b values for the two groups was not significant.

It is pointed out that although the effect of flight inhibiting factors has been defined for the various groups of Anophelines recaptured it may not be maintained very far beyond the 1 mile limit that owing to the wide fluctuations of the observed captures estimates based on the equations for distances within the 1 mile zone are subject to a considerable standard error and that effective female flight range leading to malaria transmission is dependent on the number of females coming to rest in human habitations. Adjustments must be made of density estimates based on animal trap catches before such a figure can be obtained.

HUFFAKER C B & BACK R C A Study of the Effective Flight Range, Density, and Seasonal Fluctuations in the Abundance of *Anopheles quadrimaculatus* Say in Delaware. Amer J Trop Med 1945 Mar v 25 No 2 155-61 5 figs [14 refs.]

A. quadrimaculatus is very abundant at Fort duPont Delaware but its breeding places are almost exclusively confined to two large freshwater marshes. Four cattle barns were selected at each of six distances from the nearest point of major breeding each distance was therefore replicated four times. On an average 17 inspections were made of each barn during the summer with the following results —At 0.1 miles from the breeding centre an average of 4,963

anophelines were captured per inspection at 0.5 miles 2,506 at 1.0 miles, 250 at 1.5 miles, 10 at 2.0 miles 4 and at 3.0 miles 3. The following is quoted from the author's summary:

"4 *quadrimaculatus* does not move in significant numbers more than 1 mile from its breeding sources. However an unusual condition is described where this species was observed to move 1 mile from its breeding areas in sufficient numbers to create a dangerous density—250 females per barn or shed per inspection. Near the sources of production, densities as high as 15 000 to 25 000 females per station per inspection are noted as very common, and one such record of 40 000 is included. In the study-locality (Fort duPont Delaware) broods of this species are indicated at about monthly intervals during the summer season.

R. M. Gordon

KNIGHT K. L. & FARNER, D. S. A Correction in Anopheline Nomenclature (Diptera: Culicidae) *Proc. Ent. Soc. Wash.* Washington, D.C. 1944 v. 46 No. 5 132-3. Summary taken from *Rev. Applied Entom.* Ser. B. 1945 May v. 33 Pt. 5 79.

The authors conclude from a study of the literature and of material collected over a period of more than a year in the coastal areas of the Islands of Efate and Espiritu Santo and on one occasion on Mallicolo Island that the subspecies or variety of *Anopheles punctulatus* Dön. known as *moluccensis* Sw. & Sw. in the New Hebrides and in which the proboscis excluding the labella is entirely dark, should be designated *A. punctulatus farauti* Lav. It was the only form seen there. It is not possible to say whether *A. p. moluccensis* is a synonym of *farauti* but it is anticipated that this will prove to be the case. Examination of several hundred specimens from the Solomon Islands and eastern New Guinea supports the theory but de Rook indicates that a considerable variation in the colour of the proboscis exists in western New Guinea, where most of the females determined by him as *moluccensis* have a ventral pale area on the apical quarter of the proboscis.

PARENT M. & DEMOTTE M. L. La faune anophélienne à Yangambi (Indaq) Biologie 1 *moscher* Evans spécialement Applications statistiques [The Anophelines of Yangambi. Biology of 1 *moscher*. *Rev. Tricent. Sci. III Congo Belge* 1945 Jan., No. 3 159-73 2 figs.]

PERVASSI A. Os *Kertessia* na epidemiologia da malária. Anophelines of the Sub-Genus *Kertessia* in the Epidemiology of Malaria. *Folia Med.* 1943 Dec. 5 v. 24 No. 23 213-15.

Two species of the sub-genus *Kertessia* are found in the mountains and coastal areas of Brazil: *A. (K.) cruzi* and *A. (K.) bellator*. Both are of importance in the epidemiology of malaria. The author describes the distinguishing morphological features of these two species and of *A. (K.) boliviensis* and summarizes the considerable literature concerning their habits and the rôle they play in the transmission of malaria. *A. (Kertessia) cruzi* Dvar and Knab 1908 is synonymous with *Anopheles latris* Theo. (1901) and with *Myzomyia latris* Pervassi 1908.

Norman White

OFFICER, R. Experimental Transfusion with Malaria Infected Blood. *Med. J. Australia* 1945 Mar. 17 v. 1 No. 11 271-4 1 fig.

It has long been known that malaria produced by the injection of infected blood is readily controlled by quinine but warnings have frequently been published against the use of potentially malaria infected individuals as donors.

for blood transfusion. The experiments described were carried out to determine whether the malaria acquired by blood transfusion can be readily controlled and whether the immediate harmful effects are such as to nullify the benefit of transfusion.

Five healthy volunteers who had never lived in malarious areas were the subject of experiment. Blood sufficient in amount to contain 300 000 000 parasites was drawn from a malaria patient and mixed with 560 cc of citrated blood from a compatible non malarial donor. The subject of experiment was then bled to an amount of 750 cc or until signs of collapse were noted. The malaria infected blood was then given by the drip method. All volunteers were given antimalarial treatment immediately after the transfusion the routine course of malaria therapy being used in most cases. None of the volunteers developed malaria and no immediate effects were noted. Remote effects slight to moderate pyrexia lasting one to three days—rarely began before 24 hours had elapsed and were never serious enough to cause alarm. It is concluded that in a case of emergency a potentially malarial donor can be used for transfusion with the knowledge that the benefit from transfusion would far outweigh possible ill effects. Such blood would contain less numerous parasites than did the blood used in these experiments. *Norman White*

RIGDOY R. H. A Consideration of the Mechanism of Splenic Infarcts in Malaria. *Amer J Trop Med* 1944 Nov v 24 No 6 349-54 7 figs [14 refs]

A study of the spleens of man infected with *P. falciparum* of monkeys infected with *P. knowlesi* of canaries infected with *P. cathemerium* and of ducks infected with *P. lophurae* has led to the conclusion that the infarcts occurring in the spleen in malaria may result from an obstruction produced by hyperplasia of the reticular like cells in the walls of the venous sinuses. Leucocytes and red blood cells may adhere to the surface of these masses of reticular like cells. This process is facilitated by the slowing of the blood current resulting from anaemia and anoxia of the cardiac muscle. Associated with anoxia there may be also an increase in capillary permeability. The hyperplasia of the cells in the wall of the veins is a part of the general process of hyperplasia of the splenic pulp.

[Observations on the adhesion of red cells to each other and on the adhesion of leucocytes to capillary endothelial cells were reported by HENSELY *et al* this *Bulletin* 1943 v 40 584 and may have a bearing on the subject.]

Norman White

HEIDELBERGER M & MAYER M. M. Normal Human Stromata as Antigens for Complement Fixation in the Sera of Patients with Relapsing Vivax Malaria. *Science* 1944 Oct 20 359-60

It was noted by KLIGLER and YOELI [this *Bulletin* 1942 v 39 255] that the sera of certain malarial patients fixed complement with antigens prepared from normal chicken erythrocytes. The authors of the present note find that these sera fix complement even more readily when an antigen prepared from normal human erythrocytes is employed. Furthermore many sera from malarial patients which fail to react either with *Plasmodium knowlesi* or *P. gallinaceum* antigens or with normal chicken erythrocyte antigen fix complement strongly with the human erythrocyte antigen. On the whole it may be stated that the readily available normal human stromata are about as sensitive as the *P. gallinaceum* antigen which is expensive and not easily accessible. Thus of 167 sera from malarial patients 22 per cent. were positive with the latter antigen and 28 per cent with the former. Of 32 normal sera and 81 pathological

sera tested as controls with the human erythrocyte antigen, only four probable false positives were found in all of which a malarial factor was unlikely to have been the cause. A fuller account of the observations is promised.

C. V. Henry

POTTER, H. W. BRONSTEIN, L. H. & GRUBER, C. M. Blood and Spinal Fluid Tests for Syphilis in Malarial Patients. *J. Amer. Med. Ass.* 1945 Mar 24 v 127 No. 12, 699-701

In view of the known fact that false positive serum tests for syphilis are not uncommon in malarial patients the authors tested the blood and c.s.f. of 100 consecutive malaria admissions within 48 hours of entrance to hospital. [It is not stated how many of these patients were pyrexial at the time.] All were without history of syphilis and had had at least one negative serum test for syphilis (and often several) and had passed at least 24 physical examinations it can be assumed, therefore that they were all non-syphilitic. Of the 100 sera 12 gave a positive reaction to the Wassermann and/or Kahn test and 10 a doubtful reaction to one or both tests as shown in the following table —

Positive Tests		
Kahn positive	Wassermann positive	3
Kahn positive	Wassermann doubtful	2
Kahn positive	Wassermann negative	2
Kahn negative	Wassermann positive	5
Total		12
Doubtful Tests		
Kahn doubtful	Wassermann doubtful	4
Kahn doubtful	Wassermann negative	1
Kahn negative	Wassermann doubtful	5
Total		10

The spinal fluid W.R. was negative in all cases. In one fluid there were 17 cells—6 polymorphonuclears and 11 lymphocytes per cmm. In 3 cases the total protein was 75 mgm. per 100 cc. All other tests including the Lange, were within the bounds of normality.

All serum reactions returned to negative within 30 days with an average of about 12 days. Many did so in seven days or less. All the patients had *Plasmodium vivax* infections except one in whom the infection was with *Plasmodium falciparum*. Another table as follows shows the correlation of the duration of infection and area of origin with the serological test —

Result of Test in Relation to Origin of Infection

Area	Cases	Positive	Doubtful	Average duration of infection months
Solomon Islands	49	3	5	17
Mediterranean	32	5	3	9
New Guinea	13	3	2	9
Panama	4	0	0	
West Africa	1	0	0	
Central Africa	1	1	0	
Total	100	12	10	

The conclusion to be drawn is that the physician should be wary of diagnosing syphilis on the result of one test and if the patient has had malaria particularly so a repeat test should be done after a month [Most people consider that tests if positive should be carried out over even longer periods.]

T E Osmond

MERRILL, B. R. Psychogenic "Malaria." *US Nav Med Bull* 1945 Jan. v 44 No 1 69-72.

The author has observed several patients in whom what appeared to be malarial chills proved to be anxiety attacks. In each instance *P. vivax* malaria had been contracted in the South Pacific and in each case the malaria had run a refractory course with numerous recurrences. The patients were psychologically attuned to frequent true malarial chills. Such a patient enters hospital stating that he has had a malaria chill. Shortly after admission he has another "chill" which resembles a malarial attack but there is no elevation of temperature. No plasmodia can be found. The patient resents the information that he is not suffering from malaria. The psychological history in these cases is one of psychopathic behaviour from early youth. The patient's outstanding conflict in life has been his inability to control his aggressive tendencies even before the intense accentuation of this conflict brought about by fighting and military discipline. With a sufficiently slow and tactful approach these patients may be made to accept the psychogenic nature of their symptoms the chills then disappear. There remains however a personality that has difficulty in adjusting itself to the social restraints of civilian life. The ultimate prognosis depends more on the severity of the personality defect prior to the exposure to battle than on the severity of combat experience. Psychotherapeutics of these cases are difficult largely because the psychogenic factors were so effectively concealed behind the diagnosis of malaria at the time when psychotherapy would have been most effective.

Norman White

VISWANATHAN R. Cerebral Malaria. Pathogenesis, Symptoms and Treatment. *Indian Med Gaz* 1944 Oct v 79 No 10 455-8 5 figs on pl 21

During a period of 4 months 2,256 cases of malaria were treated of which 996 were *P. falciparum* infections. Of the latter 44 patients developed cerebral symptoms eight of them died in spite of energetic anti malaria therapy. The symptomatology of the cerebral cases is described and case reports are given of the eight fatal cases together with macroscopic and histological post mortem findings. All this is preceded by a discussion of the pathogenesis of cerebral malaria. The author's observations lead to the conclusion that primary damage to capillary endothelium is caused by malarial toxin and that this leads to clumping of cells and pigment the presence of parasites in the cells is immaterial. The slowing of circulation due to the fall of blood pressure in the later stages of cerebral attacks facilitates the process of thrombosis and irreparable and irreversible damage is done to the brain tissue. In five of the fatal cases a well formed ante-mortem clot was found in the sagittal sinus. The author believes that sinus thrombosis in cerebral malaria has not hitherto been reported.

All the non fatal cases of cerebral malaria ended in complete recovery.

[For a description of the pathological findings in cerebral malaria and a discussion of the processes involved see DHAYAGUDE and PURANDARE this *Bulletin* 1944 v 41 533]

Norman White.

GORDON H. H., LIPPINCOTT S. W., MARRIE, A., BALL, A. L. ELLERBROOK, L. D. & GLASS W. W., Jr. Clinical Features of Relapsing *Plasmodium vivax* Malaria in Soldiers Evacuated from the South Pacific Area. *Arch Intern Med* 1945 Mar., v 75 No. 3 159-67 5 figs.

The observations concern 435 soldiers evacuated to the United States from islands in the South Pacific mostly on account of frequent relapses from malaria. All but seven were white all were young adults with the exception of 20 none had suffered from malaria prior to exposure to infection in the South Pacific all had had suppressive treatment in the Pacific, mostly with quinaquine hydrochloride (mepacrine) 0.4 or 0.6 gm. weekly all had had prompt treatment of acute attacks all but four had had acute attacks prior to admission to the Harmon General Hospital where these observations were made (and where the incidence of indigenous malaria is extremely low) all were observed from one to seven months. *P. vivax* alone was found in all but one patient, in whom *P. falciparum* was also identified.

The strain or strains of *P. vivax* were characterized by a very pronounced tendency to relapse and to the relative mildness of the acute attacks they caused. Of 49 men the duration of whose infection was from 13 to 18 months 37 per cent. had had from 10 to 12 attacks 12 per cent. had had from 13 to 16 attacks and two men had had more than 16 attacks.

The symptoms displayed by these patients are analysed in some detail. Chill was experienced in 80 per cent. headache weakness and malaria in 96 per cent. abdominal pain in 47 per cent. nausea in 59 per cent. vomiting in 56 per cent. herpes labialis in 27 per cent. Cerebral symptoms were conspicuously infrequent, and when they did occur were probably conditioned as much by the previous personality of the patient as by the effects of the malaria attack. Splenomegaly was not marked the spleen was felt in 23 per cent. of acute attacks but then only transiently.

Most of the clinical attacks were treated with quinaquine hydrochloride, 0.2 gm. every six hours for five doses then 0.1 gm. thrice daily for six days. In only one patient was the response to quinaquine given by mouth unsatisfactory.

A programme of rehabilitation was instituted, with great benefit to the development of physical stamina and the restoration of self-confidence.

Norman White

WAR OFFICE. ARMY MED DEPT BULL. No. 48. 1945 June 6-7 Drugs for Relapsing Vivax Malaria.

"Radical cure of malaria is the permanent elimination of infection and the criterion for its attainment is freedom from relapses.¹ Anti-malarial drugs vary in their ability to produce a radical cure and their effectiveness in this respect can be tested by comparing relapse rates after different forms of treatment. Reinfection will obscure the anti-relapse properties of the best drug therefore trials were carried out in the United Kingdom on men returned from the Central Mediterranean Force who developed relapses of malaria. Practically all relapses were due to vivax (B.T.) malaria since continued use of mepacrine for 3-4 weeks after leaving the malarious area had eliminated falciparum (M.T.) malaria only proved cases of relapsing B.T. malaria are considered here. During May and June 1944 1410 such cases were treated with one or other of the two courses below—

"(1) *Mepacrine (M) course*.—0.2 gram of mepacrine was given every six hours for 48 hours—then 0.1 g. three times a day for 10 days. The course lasted 12 days and the total amount of mepacrine was 4.6 g.

(2) *Quinine pamaquin (QP) course*—Quinine grains 10 and pamaquin 0.01 gram were given three times a day for ten days.

Records were examined after a follow-up five months later*. In 176 of the patients the first attack of malaria developed after their return to this country. Of these 100 were treated with course M and 29 subsequently relapsed. 76 were treated with the QP course and only 14 relapsed within the period of observation.

The difference between these relapse rates is statistically significant; this means that the odds are heavily against such a result having happened by chance alone and other things being equal strongly suggests that the QP course of treatment was the more effective in preventing relapses.

TABLE.—*Relapses of vivax (B T) malaria after treatment with mepacrine or quinine pamaquin courses*

Relapses after treatment	Course M		Course QP	
	No. of cases	Percentage of all cases	No. of cases	Percentage of all cases
None	429	66.0	524	89.7
1	184	28.3	56	9.6
2	33	5.1	4	0.7
3	4	0.6	0	—
Total relapsed cases	221	34.0	60	10.3

Men whose first attack had developed abroad formed a much larger group (1,234 cases). They also were treated with course M (850 cases) or course QP (584 cases) and again the follow up showed fewer relapses after QP treatment; the findings are given in the table.

Further analysis revealed an unexpected event—namely that relapse after the QP course when it did occur was earlier than after course M; the explanation of this difference is not known although in part at least it may be due to the slower excretion of mepacrine.

This follow-up was carried out five months after the patients had been treated, so far the QP course appears to have been more successful than course M, but it is too early to say that radical cures have been obtained since BT relapses may occur up to two years after the last infection.

Two points of importance must be borne in mind in treating patients with the QP course. The first is that the patient must be kept under strict medical supervision throughout treatment and if cyanosis or abdominal colic appears pamaquin should be discontinued and the course completed with quinine only; only some 2–4 per cent had to have treatment interrupted in this way. The second is that Indian troops do not tolerate pamaquin as well as British; for this reason Indians should receive only 0.02 g. instead of 0.03 g. of pamaquin daily. Pamaquin haemoglobinuria has been described in Indians; it appears usually on the 4th or 5th day after pamaquin has been started. It should be treated like blackwater fever.

*War Office, 1945 D.B.R. *Interim Report on Malaria Relapses after Treatment with Quinine and Synthetic Quinine Substitutes*.

SIXTON J. A. The Principles governing the Curative and the Suppressive Treatments of Human Malaria, with special references to Military Conditions. *J. Roy. Army Med. Corps* 1945 Apr., v 84 No. 4 147-58. [16 refs.]

A successful chemotherapeutic attack upon the gametocytes or sporozoites of malaria in man would be prophylactic, preventing the transmission of infection either to the mosquito or man. A similar attack upon any stage of the asexual cycle of the parasite would be a curative action. In discussing malaria therapy exact definitions should be given of the terms used.

Direct gametocyte prophylaxis is the prevention of the development of infection in the insect vector by the direct destruction, sterilization or devitalization of the gametocytes before they leave the human host.

Indirect gametocyte prophylaxis refers to the temporary reduction in the number of gametocytes or the temporary elimination of these forms in the peripheral blood, by the destruction of the asexual parasites from which they derive.

Eventual gametocyte prophylaxis is the permanent elimination of gametocytes by the complete eradication of the schizontic forms from which they derive.

True causal prophylaxis entails the radical destruction of all introduced sporozoites or the hypothetical cryptozoites.

Suppressive treatment is designed to prevent the development of clinical malaria by means of continued drug treatment.

Clinical cure is the cure of clinical manifestations of malaria.

Radical cure is the permanent elimination of infection.

In the light of these definitions the action of the commonly used anti-malarial drugs—quinine, mepracrine and pamaquin—is described. Reference is made to experience in highly malarious areas in New Guinea where it has been shown that the administration of 0.1 gm. of mepracrine every day without fail to all personnel enables a military force to maintain itself in the field with a very low malarial attack incidence.

The applications of the principles of malaria therapy under different conditions of military service are thus summarized.

For non-infected individuals coming to reside in an area where the chances of acquiring malaria infection are slight, no suppressive treatment is necessary. Primary acute attacks should be submitted to radical treatment of short duration, with occasional gametocyte therapy for *falciparum* infections. Relapsing infections necessitate a repetition of the standard course. Special treatment being required for chronic malar infections.

For individuals coming to reside in a non-malarious or slightly malarious region from a highly malarious one and if the period of absence from risk of heavy infection is likely to be prolonged suppressive treatment may be stopped after four weeks. Primary acute attacks and relapsing infections should, however, be treated as in the previous category. If the period of absence from the risk of heavy infection is likely to be short, suppressive treatment should be continued without cessation.

For individuals exposed to constant and frequent infections, reinfections and superinfections, the treatment should vary in accordance with their state of immunity to malaria. If much malaria sickness occurs in an immune or partly immune population, suppressive treatment with mepracrine in moderate doses should be given. This can often be discontinued after a few months. Attacks of fever should be so treated as to secure a rapid clinical, but not radical, cure. Gametocyte therapy or light suppressive treatment is sometimes indicated to protect adjacent non-immune troops. For non-immune or partly immune troops in such conditions continuous suppressive treatment in full doses should be given.

even if there be a break in the malaria transmission season attacks should be treated with a short intensive course. Norman White.

MEASHAM J E YOELI M & FINNEGAN J D *An Inquiry into the Prophylactic, Suppressive and Curative Properties of Mepacrine (Atebrin)* *J Roy Army Med Corps* 1945 Apr v 84 No 4 188-91

Seventeen patients in a mental hospital in Lebanon were the subjects of the inquiry. Eight received a three weeks course of suppressive mepacrine 0.4 gm. twice weekly. At the end of this period they were infected with Palestinian or Syrian strains of *P. vivax* by mosquito bites *A. zacharovi* and *A. superpictus* and by subsequent subcutaneous injection of the remaining sporozoites obtained by dissection in saline. The patients continued the suppressive treatment for another month during which a second dose of sporozoites was administered to each.

A second group of eight patients similarly infected, only started their suppressive treatment on the day of their experimental infection.

The remaining patient was a control. He received one injection of sporozoites but no suppressive treatment.

Five patients of the first group and three of the second group developed clinical malaria all but one after the cessation of the suppressive treatment.

The field observations reported concern a battalion of Indian infantry in a highly malarious frontier zone where anti larval measures were not possible. Another battalion stationed in the same area in the previous year in exactly similar conditions had received no suppressive treatment. It suffered severely from malaria 180 cases of malaria being reported in a single week of July. The battalion under observation was on carefully controlled suppressive mepacrine treatment only two cases of malaria occurred. On withdrawal to a healthy camp half the strength ceased taking mepacrine immediately the other half continued taking it for a further month. Malaria cases in the former group equalled 17 per cent of strength there was no case among the men who continued the suppressive treatment for a month after removal from the malarious area. [It is not stated if *P. falciparum* infections were common in this area or if the malaria which occurred after the cessation of mepacrine suppression was due entirely to *P. vivax*].

The following conclusions are reached — Mepacrine is not a true prophylactic but it is a useful suppressant. If continued for a sufficient period mepacrine cures infections at a subclinical level. Norman White

THOMPSON J H *Large Initial Doses of Atebrin in the Treatment of Benign Tertian Malaria.* *J Trop Med & Hyg* 1944 Dec.-Jan. 1945 3 pp

This is an account of the treatment of a hundred American soldiers who had contracted malaria in the Mediterranean area and who developed clinically active *P. vivax* malaria after their transfer to a non malarious temperate clime. All but four gave histories of having suffered from malaria during the previous summer but their transfer was not made on health grounds. It was not possible to distinguish relapses from latent infections. In the 100 cases the histories revealed an average of 2.4 relapses since the first attack six to nine months previously the number of relapses varying up to twelve.

Seventy-eight patients received unusually large doses of atabrine [mepacrine] an initial dose of 0.6 gm. followed by 0.2 gm. after each meal for six doses and then 0.1 gm. thrice daily for seven days. The remaining 23 patients received 0.2 gm. every four hours for five doses and then 0.1 gm. thrice daily for five days.

Atabrine was always given after meals, and if the initial dose had to be given before meal time it was preceded by a pint of chocolate milk, fruit juice or egg nog.

During a two-month period eight patients relapsed of these only three, 4 per cent., had received the large initial dose of atabrine. There were no toxic manifestations in any case sufficiently severe as to necessitate stopping the medication. 15 per cent. had mild diarrhoea early after the initial large dose. 6 per cent. had mild diarrhoea early controlled by paregoric. No patient had mental symptoms.

The eight patients who relapsed were given an initial dose of 1 gm. of atabrine, followed by 0.2 gm. every four hours for six doses and then 0.1 gm. thrice daily for a week. About 6 hours after the 1 gm. dose the patients had severe chills. Before that, marked disintegration of the parasites was observed. Dumping of pigment in the plasmodia was observed as early as 45 minutes after the taking of the large dose. Four of the patients had nausea, one had marked diarrhoea and one had mental symptoms with high fever both transitory. This large 1.0 gm. initial dose should be reserved for selected cases. The optimum time to give a large initial dose is 24 hours after a chill when the patient is having tertian fever.

SMITH, G. C. & PASSALACQUA, L. A. Treatment of Acute Malaria with Heavy Doses of Atabrine, *Bol. Asoc. Med. de Puerto Rico* 1944 Sept., v. 36 No. 9 390-97. 74 refs.

The authors report favourably on the treatment of 10 cases of acute malaria with large doses of atabrine mepracrine. During the first 24 hours of treatment the patients received 1.2 gm. of the drug, four doses each of 0.3 gm. During the following four days another 1.2 gm. are given, the total amount given in the five day treatment being 2.4 gm. With this treatment half of the patients with *P. vivax* infections had only one day of fever. The results compared favourably with those obtained by quinine treatment. Eighty-three per cent. of the mepracrine patients with *P. vivax* infections had neither fever nor symptoms of malaria after the first forty-eight hours. Mepracrine was never given on an empty stomach. Tea or fruit juice with much sugar was given before the drug was administered. *P. falciparum* infections did not respond to mepracrine as rapid as did *P. vivax*.

See also p. 753. MARRIOTT. Medical Problems of South-East Asia Command

KAY, C. F. Failure of Mepacrine as an Adjuvant to Atabrine in the Treatment of Relapsing Tertian Malaria. *J. Amer. Med. Ass.* 1945 Apr. 14 v. 127 No. 15 984. 1 chart.

In the Far East 178 patients suffered from relapsing *P. vivax* malaria during a period in which the incidence of fresh infections was insignificant. January to March inclusive. Of these, 109 were treated with atabrine [mepacrine] 0.2 gm. every six hours for five doses then 0.1 gm. thrice daily for six days. A further relapse occurred in 74.3 per cent. of these patients during the 85- to 140-day period of observation.

In addition to this mepacrine treatment 67 patients were given three intravenous injections of mepacrine, 0.04, 0.06 and 0.06 gm., on the third, fifth and eighth days of mepacrine treatment. 71.6 per cent. of these patients relapsed again. Very early further relapses were slightly more frequent in the group treated by mepacrine alone.

It is concluded that mapharsen given in the above dosage is of no value as an adjuvant to mepacrine in the treatment of relapsing *P. vivax* malaria

Norman White

DAO L. LUIS Resultados clínicos obtenidos con el Mafarside en el tratamiento del paludismo [Clinical Results obtained with Mapharside in the Treatment of Malaria.] *Rev Policlínica Caracas* 1944 Sept-Oct v 13 No 78 339-49 2 figs. English summary

The author reports favourably on the value of mapharside as an antimalarial drug. Sixteen patients with acute malaria, 15 *P. vivax* and one *P. falciparum* infection were treated. Each patient received three intravenous injections the adult doses being 0.04 gm. for the first injection and 0.06 gm. for the other two. The interval between the first and the second injection was four days and between the second and third five days. The results were favourable in all the *P. vivax* infections in 13 cases the fever ceased after the first injection. Only three of the patients suffered from a relapse during a two-month period of observation after the end of treatment. The patient with the *P. falciparum* infection developed serious symptoms and received quinine therapy.

Twelve patients with relapsing malaria were treated 11 *P. vivax* and one mixed infection. They each received 8 intravenous injections of mapharside at intervals of six days the first 0.04 and the remainder 0.06 gm. The results were good. A marked improvement in the general health of the patients and the reduction of the spleen to normal limits were noted. Only two patients had a further attack of fever during three months following treatment.

Eighteen chronic cases of malaria splenomegaly 11 of them being afebrile were treated with an association of typhoid paratyphoid vaccine and mapharside. Six of the cases with very pronounced anaemia received preliminary treatment with liver extract and iron. One cc. of typhoid paratyphoid vaccine was given weekly for eight weeks on the day following these injections mapharside was given intravenously as in the acute malaria cases. In six cases the febrile reaction caused by the vaccine was very intense in these subsequent doses of vaccine were lessened. There was marked improvement in the general health of all patients. The pain so commonly associated with great enlargement of the spleen disappeared after the first injections. There was noteworthy reduction in the size of the spleen in three cases slight reduction in two no apparent reduction in 10. Three patients did not complete the treatment.

Before using mapharside or any other trivalent arsenical a thorough examination of the patient is necessary to exclude contraindications to their use

Norman White

UNTI O Dosagem da quinina e da quinidina no sangue. (Contribuição para a simplificação da técnica de extração e avaliação de alguns alcalóides da quina.) [Estimation of the Quinine and Quinidine Content of the Blood. Contribution towards the Simplification of the Technique of Extracting and Estimating Cinchona Alkaloids.] *Arquivos de Hig e Saúde Pública* São Paulo, 1944 Sept. v 9 No 22 35-48. English summary

Quinine when treated with sulphuric citric or tartaric acid, displays a blue fluorescence when exposed to the ultra violet rays from a mercury vapour lamp with a special filter. This fluorescence disappears if hydrochloric acid be added to the solution. These facts are the bases of the author's method of estimating the quinine content of the blood a method for which simplicity and accuracy are claimed. The method is described in detail.

One cc. of blood is mixed with 3 gm. of anhydrous sodium sulphate triturated and transferred to a flask of 25 cc. capacity. The flask is placed in a water bath

and four or five drops of concentrated liquid ammonia are added to alkaline the quinine salt. The alkaloid is extracted with 8 cc. of chloroform-ether 8 part of chloroform to two of ether in a water bath at 65°C. When the chloroform-ether is reduced to about one third of its volume it is cooled and decanted into another flask. Five cc. of chloroform-ether are then added to the residue in the first flask and the operation repeated, three times in all. The chloroform-ether from these three extractions is then evaporated to dryness. To the residue 2 per cent. sulphuric acid is added to make a solution of 1 cc., the volume of the blood used. The fluorescence exhibited by this solution when exposed to ultra violet rays is compared with that given by solutions of quinine of known titre.

By this means quinine can be detected in blood when present in dilutions as great as one in 6 000 000

Norman White

COGGESHALL, L. T. MARTIN, W. B. & BATES, R. D. Jr. Sulfadiazine in Treatment of Relapsing Malarial Infections due to *Plasmodium vivax*. *J. Amer. Med. Ass.* 1945 Mar 5; 128 No. 1 7-8.

This report shows that sulphadiazine was of no value in preventing relapses in *P. vivax* malaria infections naturally acquired in the South-west Pacific area.

Thirty three unselected patients suffering from relapsing *P. vivax* malaria were given antimalarial therapy 30 with atabrine (mepacrine) 0.1 gm. three daily for seven days and three with quinine. On the eighth day sulphadiazine treatment was begun, 8 gm. on the first day and then 1 gm. every four hours night and day for a week. For a second week the dose of sulphadiazine was reduced to 1 gm. every six hours night and day. An attempt was made to maintain a blood level of 8 to 10 mgm. sulphadiazine per 100 cc. during the first week. There were no toxic manifestations other than mild microscopic haematuria in three patients "this cleared after increase in the fluid intake and alkalification of the urine. Within three months 16 of these patients (48.5 per cent.) had had further relapses. The corresponding relapse rate of 134 patients who had had similar antimalarial treatment but without sulphadiazine was 48.2 per cent. The average blood concentration of sulphadiazine of the 16 patients who relapsed had been 7.7 mgm. per 100 cc. that of the 17 patients who had not relapsed by the end of three months had been 7.6 mgm. per 100 cc.

Norman White

COLLIGNON, E. La campagne antipaludique de 1943 dans le département d'Alger [The Anti-Malaria Campaign of 1943 in the Department of Algiers.] *Arch. Inst. Pasteur d'Algérie* 1944 June v 22, No. 2, 131-40.

The presence in the Department of Algiers of a large number of troops most of whom were unprotected against malaria by previous exposure obliged the antimalaria organization to concentrate all its resources on preventive measures throughout 1943. The usual epidemiological investigations had to be renounced. Fortunately the year was favourable. Deficient rainfall that had characterized the winter continued throughout the first half of 1943. The usual spring breeding places of anophelines were fewer and smaller than usual. The autumn rains were early, abundant and persistent and flushed many other habitual breeding places. *A. maculipennis* [probably *labranchiae*] the chief vector was less in evidence than usual. During the summer in the mountains *A. bifurcatus* and *A. mariti* were found sharing common breeding places. With the assistance of the hydraulic services extensive antilarval work was carried out. In spite of the presence of an abnormally large susceptible population and a shortage of antimalarial drugs there were only localized outbreaks of malaria once summer

had set in and these outbreaks were mostly quenched early in the autumn. The number of parasite carriers probably increased, however owing to the insufficiency of drugs for adequate treatment a fact which made the outlook for 1944 somewhat disquieting

Norman White

SEELER A O The Inhibitory Effect of Pyridoxine on the Activity of Quinine and Atabrine against Avian Malaria. *J Nat Malaria Soc* Tallahassee Fla. 1945 Mar v 4 No 1 13-19 1 fig

The fact that para-aminobenzoic acid which is necessary for the growth of certain bacteria inhibits the action of the sulphonamides is in support of Wood's hypothesis that the sulphonamides act by displacing para-aminobenzoic acid and thus depriving the bacteria of its use. On the assumption that drugs such as atabrin and quinine owe their antimalarial activity to the fact that they similarly displace some substance essential to the growth and survival of the parasites the author decided to carry out tests on the effect of large doses of vitamins. In this paper he shows that pyridoxine administered orally or subcutaneously definitely inhibits the action of both quinine and atabrin on *Plasmodium lophurae* and *P. cathemerium* in Pekin ducklings and another unnamed avian parasite in some other host. The daily dose of pyridoxine was 500 mgm per kgm of bodyweight for oral administration and 200 mgm. when given subcutaneously. The drugs were administered into the crop in aqueous solution once daily. The degree of inhibition as judged by the percentage of infected erythrocytes on certain days varied with the dose of the drug. When the dose was the minimal effective dose inhibition was practically complete but with increasing dosage the inhibiting action of pyridoxine in the quantities employed became less marked. Thus with a dose of quinine of 10 mgm/kgm there was complete inhibition, whereas with a dose of 15 mgm./kgm. there was only a slight inhibitory action. It was thought that pyridoxine might influence the toxicity of quinine and atabrin. Experiment on mice showed, however that the toxicity was in no way influenced even by the administration of massive doses of pyridoxine. How pyridoxine acts is unknown, for there is no information available as to whether this substance plays any part in the metabolism of avian malarial parasites. The author thinks it probable that both quinine and atabrin owe their antimalarial activity at least to some extent to their interaction with pyridoxine or a pyridoxine like substance. [Compare the work by TRAGER on biotin deficiency in relation to *P. lophurae* infections this *Bulletin* 1943 v 40 676 825]

C M Wenyon

COGGESHALL, L. T. PORTER R. J & LAIRD R. L. Prophylactic and Curative Effects of certain Sulfonamide Compounds on Exoerythrocytic Stages in *Plasmodium gallinaceum* Malaria. *Proc. Soc Exper Biol & Med* 1944 Nov v 57 No 2 286-92.

Although quinine and atabrin are effective against blood forms of *P. gallinaceum* in chicks they are inactive against exoerythrocytic stages of the parasite. According to KIKUTH & MUDROW [this *Bulletin* 1940 v 37 188] plasmoquine has some effect against the latter. The study of drug action on exoerythrocytic forms offers some difficulty since they are not numerous in the blood. A simple biopsy method allowing multiple examinations of brain tissue in each bird, without causing much damage is described in this preliminary report. The developmental course of exoerythrocytic forms in treated and control birds can readily be followed. Recently an investigation of a similar nature has been reported by COATNEY & COOPER [this *Bulletin* 1945 v 42, 353]. White Rock chickens were inoculated with about 20 000 sporozoites obtained from—

the salivary glands of infected *Aedes aegypti* and suspended in 0.2 cc. of heparinized normal chick blood. For brain biopsy a small syringe of 0.25 cc. capacity fitted with a 20 gauge needle and containing 0.02 cc. saline was used. The needle was pushed into the brain cortex and rotated through a complete circle while applying slight suction and by this means enough material for examination of a stained film was obtained. Following routine infection with sporozoites the exoerythrocytic forms first appeared in brain capillaries 7-8 days after inoculation the period was shortened by giving larger inocula. After inoculation of infected blood cells these forms appeared much later. Some spontaneous recoveries were noted by the above biopsy method after exoerythrocytic forms had appeared in the brain.

In one experiment, after the appearance of exoerythrocytic forms in the brain, following inoculation of infected blood sulphaguanidine, sulphapyridine, sulphathiazole, sulphadiazine, sulphanilamide and quinine were given to the chicken host by mouth. Of a total of 13 birds which received the sulphonamide drugs in doses of 250-500 mgm. daily over a period of days starting when exoerythrocytic forms were first seen 10 recovered and three died three others which received 40 mgm. of quinine daily also died. Each of four controls had exoerythrocytic forms in the brain two died and two recovered. It was possible to pick out effective drugs early in treatment because of the altered appearance of the exoerythrocytic forms. When the experiment was repeated a number of times quinine and atabrin and many other compounds were found to be ineffective while plasmoquine and 4,4-diaminodiphenyl sulphone were only weakly effective. A number of drugs were also tested on sporozoite infections of the chicks. Sulphadiazine alone or with quinine prevented the appearance of exoerythrocytic forms. If drug treatment was withheld until after exoerythrocytic forms had appeared in the brain, sulphadiazine and sulphapyridine [sulphapyrazine is given in the table] destroyed them while quinine and atabrin again proved inactive.

J. D. Fallon

BLACKWATER FEVER.

BIENBAUM D. GOLDBLUM N. & KLIGLER I. I. The Sensitivity of Malarial Blood to Hemolysis. *Harefuah* Jerusalem 1945 May 15 v. 23 No. 10. [In Hebrew 213-17 (10 refs.) English summary 217]

1. The administration of quinine to healthy adults for seven days has no influence either on the red cell or reticulocyte counts or on the rate of hemolysis.
2. The increased sensitivity of the erythrocytes to hemolysis in bile salts persists for about two months after the malarial attack.
3. As to the hemolytic property of the drugs in the test tube it was found that atabrine and sulphanilamide are not hemolytic quinine and plasmoquine are hemolytic only in high concentration. Quinine hemolyzes in a dilution of 1:800 and plasmoquine in a dilution of 1:200.
4. Quinine atabrine and plasmoquine together with bile salts cause hemolysis. Individually in similar concentration neither the drugs nor the bile produced any hemolysis. Sulphanilamide did not influence hemolysis either in the test tube or when added to a solution of bile.
5. The addition of 0.02% NaHCO_3 to bile solution delays the hemolysis of normal and malarial blood by 1-1½ hours. The blood of patients with enlarged spleens is sensitive to hemolysis even in the absence of clinical symptoms and of malarium in the circulating blood.

8 NaHCO_3 delays hemolysis in quinine bile mixtures as well as in atabrin mixtures. A similar effect is produced by the addition of KHCO_3 or Na_2HPO_4 .

7 The neutralization of quinine delays its hemolytic activity but it seems that the hemolytic effect of a neutralized mixture of quinine and bile is greater than that of the individual substances in the same concentration. Acidity is an additional factor in producing hemolysis.

8 Serum bile and serum-quinine-bile mixtures inhibit hemolysis. Our methods of examination revealed no difference between normal and malarial serum in respect to the hemolysis of erythrocytes. The sensitivity to hemolysis depends on the erythrocytes and not on the serum.

SWANTZ H E & BAYLISS M. Haemoglobinuria. Report of Ten Cases of its Occurrence in Negroes during Convalescence from Malaria. *War Medicine* Chicago 1945 Feb v 7 No 2 104-7

Among over 2 000 patients with malaria treated in an evacuation hospital in a forward area in a malarious island ten suffered from haemoglobinuria either during or shortly after treatment. All ten were Negroes in spite of the fact that the majority of the malaria patients were of the Caucasian race. All recovered. All but one of the ten had previously had positive blood smears but at the time of onset of the haemoglobinuria all blood smears were negative. The treatment of the malaria in most of these ten patients had been with quinine, quinacrine hydrochloride (mepacrine) and pamaquin naphthoate. The authors believe that pamaquin naphthoate may have played an important rôle in the production of haemoglobinuria in some of the cases. It was not the only factor for one patient had received none at all and in some others the onset of haemoglobinuria was delayed as long as three weeks after the discontinuance of the drug. It is curious that all the patients were Negroes. The treatment of their malaria differed in no respect from that of other races. Most of the patients gave a history of having previously suffered from malaria in the southern United States.

Norman White

SINGH I & SINGH I. A Note on the Treatment of Black Water Fever with Antivenene. *J Indian Med Ass* 1945 Mar v 14 No 6 116-18

Four patients with blackwater fever were treated with antivenene and recovered. A fifth who did not receive antivenene died. In the fatal case anuria developed which did not respond to medical methods. At autopsy the lower ends of both ureters were blocked with a reddish brown clot. Three of the recovered patients had received pamaquin before blackwater fever developed. The histories of the fourth case and the fatal case are not given.

The authors recommend surgical interference (either ureteric catheterization or unilateral nephrostomy) in anuric cases which do not respond to medical treatment.

[This paper is not very carefully presented and references to the literature are often misquoted and incomplete. For example Ross (1942) is quoted as advocating pelvic lavage but the reference is not given. The section of the paper devoted to the mechanism of anuria in blackwater fever has been written without reference to the literature apart from a quotation from the *Memoranda on Medical Diseases in the Tropical and Sub-tropical Areas* 1942 which incidentally is not placed in quotation marks and is wrongly paged in the list of references. In the summary the statement 'a case of anuria was successfully

treated by ureteric catheterisation has no connexion with the present paper but apparently refers to a personal communication from Bingham (1944) mentioned in the text. The advice regarding surgical interference in blackwater fever is in the opinion of the reviewer thoroughly unsound.]

B. G. Macgregor

TRYPANOSOMIASIS

BAX S. N. Report on the Work of the Tanganyika Tsetse Research Department since February 1944. 12 pp. 2 charts. [Mimeographed report dated Shinyanga 20th Nov. 1944.]

Various observations and experiments in the field and laboratory have been continued during the past year and some new work carried out.

Tsetse in captivity—JACKSON found that *G. morsitans* which were kept in darkness at outdoor temperatures and 100 per cent. relative humidity synthesized less fat than was found in caught flies and some died with full meals of undigested blood even three days after the meal. VANDERPLANK found that feeding with either sheep or fowl blood was suitable for reproduction and longevity in *G. morsitans* (Races A and B) *G. swynnertoni* *G. pallidipes* *G. austeni* *G. palpalis fuscipes* *G. palpalis martinii* *G. longipennis* *G. fuscipennis* and *G. brevipalpis*.

A tsetse feeding apparatus designed by VANDERPLANK in which rat skin membrane defibrinated blood an electrical thermostatic heater and a centrifugal pump are used, promises to save much time and to result in greater longevity and reproduction of the flies.

Field studies—JACKSON found that inconspicuous (dark) colours gave no better survival in marked flies than conspicuous colours. VANDERPLANK continued experiments on scents: alcoholic extract of ox scent on screens doubled the catches of *G. pallidipes* and increased the catches of *G. swynnertoni* by 50 per cent. JACKSON confirmed MELLANBY's view [this *Bulletin* 1937 v. 34: 558] that humidity does not affect the metabolism of fat. BUXTON and LEWIS [ibid. 1935 v. 32: 389] and JACK [ibid. 1940 v. 37: 400] got a contrary result. The amount of weight lost by a tsetse at 25°C. and 50 per cent. R.H. was found to be almost independent of its initial weight: hence small flies are at a disadvantage. Body weight is related to wing length. Age can be determined fairly well from the fraying of the wings.

GLASGOW investigated the process of teneralization [cuticular hardening] in *G. morsitans* and concluded that the age of teneral [newly emerged] flies could be estimated by examination of sections of the cuticle. JACKSON studied the development of fat and the activity of tsetse.

When *G. morsitans* was introduced (as pupae) into a *G. swynnertoni* habitat it produced a considerable second generation unless there was a great excess in numbers of *G. swynnertoni*: but the bodily condition of *G. morsitans* was not so good as in its own habitat. *G. palpalis* did fairly well in a riverine habitat in a *G. swynnertoni* area but failed completely away from the river: it seemed to feed on reptiles only.

Work on hybrids has been continued by VANDERPLANK: ten species—*G. morsitans* (Races A and B) *G. swynnertoni* *G. pallidipes* *G. austeni* *G. palpalis fuscipes* and *martinii* *G. longipennis* *G. fuscipennis* and *G. brevipalpis*—and 1,200 tsetse have been used [see also this *Bulletin* 1945 v. 42: 99].

G. palpalis fuscipes and *G. palpalis martinii* mate at random but the male

martini always kills the female *fuscipes* with its large superior claspers when the tips of the claspers were cut off offspring were obtained. Some of the female offspring were fertile but the male offspring could not mate owing to abnormalities of the genital organs.

G. morsitans (Race B) from the Tanganyika coastal belt are genetically and morphologically different from the typical *G. morsitans* (Race A) of central Tanganyika. male hybrids between these two races or subspecies are completely sterile and the females are partly sterile when crossed back with either parent race. Race B crosses more readily with *G. swynnertonii* than with Race A and more offspring are produced. male hybrids however are still sterile and females partly so.

G. austeni is generally prevented from mating with tsetse of the *morsitans* group owing to its size but insemination of females of that group by *G. austeni* males has taken place in the laboratory but without offspring.

Other species mate outside their own species only very exceptionally.

Trypanosomes—*T. congolense* has been shown by measurements to be dimorphic and *T. rhodesiense* was found by measurements in relation to its electric charge to be tetramorphic. VANDERPLANK (below) has found an infection with *T. congolense* in a *G. austeni* female (in this report it is said to be a male).

In dissections of 30 000 wild *G. swynnertonii* and *G. pallidipes* a seasonal variation in infection with trypanosomes was found. it seems probable that a higher rate of infection occurs in the older nonteneral flies. There has also been a steady annual fall in the infection rate during the last three years and a parallel seasonal and annual change in the incidence of trypanosomal infection in game animals was noted.

From a study of the nucleus of trypanosomes VANDERPLANK concluded that there were two sexes in all species so far examined and he thinks that sexual reproduction takes place by exchange of gametes in the fly. *T. brucei* has the same number of chromosomes as *T. rhodesiense* but in the former the Y chromosome is larger and more obvious. *T. simiae* is identical with *T. congolense* [see also this Bulletin 1944 v 41 829].

Further observations on the effects of fire-exclusion and clearing of the hard pans and of selective clearing were made at Shunyanga. As selective clearing failed to eliminate *G. swynnertonii* from experimental Block 7c a hybrid experiment was made in June 1944 about 144 000 *G. morsitans* (Race A) pupae from Kondoa Irangi were introduced into the area with the result that *G. morsitans* spread all over the area and outnumbered *G. swynnertonii* by 7 to 1 in September and October. Some hybrids have been caught in the block but it is too soon to know whether the experiment will be successful in eliminating *G. swynnertonii* though a considerable reduction in its numbers has occurred.

Further clearing has been done in *G. pallidipes* areas. J. F. Corson

1. VANDERPLANK F. L. Infection of *Glossina longipennis* and *G. fuscipennis* with *Trypanosoma congolense* [Miscellanea.] Ann Trop Med & Parasit. 1945 May 31 v 39 No 1 61
2. — A Note on Wild *Glossina austeni* Infective with *Trypanosoma congolense* [Miscellanea.] Ibid. 62.

i. The author records that he succeeded in infecting both *Glossina longipennis* and *G. fuscipennis* with *Trypanosoma congolense* by allowing them to feed on an infected sheep.

ii. Four species of *Glossina* occur at Kingolwira near Morogoro Tanganyika Territory. In August 1944 the author and a native assistant dissected nearly

marinus always stained also in mice since 1933 and more virulent to these animals when the tips of strain was mentioned by P BROWNING [this Bulletin 1938 v the female offe

to abnormali reaches the fastigium or acme s.e when parasites are

G morsitans in a microscope-field about 7 or 8 days after inoculation this morphological metimes followed by the persistence of parasites in large numbers. Tanganyika in a few days a so-called acute course but more commonly by either sterile aing course with the first negative period occurring two to five days parent rne fastigium or a chronic course in which the parasites never disappear and m the blood and may persist in considerable numbers though fluctuating emaleays or weeks In order to retain unchanged the immunological character

G se strain it is necessary to pass it on from mouse to mouse at the fastigium proul a line maintained in this way is referred to as the acme strain of *T. congolense* nals. When the infection becomes relapsing-chronic and parasites after diminish

Og in the blood again become numerous this is referred to as a relapse 2stigium

b) Strain II reaches the acme stage in about five or six days after which unlike Strain I the parasites very rarely disappear or diminish to any great extent g and death supervenes from two days to several weeks later

o Section II—Treatment of Experimental *T. congolense* Infection in Mice with No 897—This compound is 7 amino-9 (p-amino-phenyl) 10-methyl phenanthridinium chloride [MORGAN and WALLS J Chem Soc 1938 389] prepared at the Chemical Research Laboratory Teddington. A dose of 1 mgm. per 50 gm. body weight is well tolerated by mice. 2 mgm per 20 gm. is fatal in about 75 per cent of cases (Throughout the drugs are given subcutaneously ch a single dose in a proportion of 1.0 cc. of aqueous solutions containing e amount stated per 20 gm. body weight.)

Strain I infections respond to treatment better than Strain II about 60 per cent of the former (treated at acme) being cured by a dosage of the order mg 0.01 mgm. as against some 40 per cent. of the latter by a dosage of the order mg 0.07-0.1 mgm. With both strains treatment is substantially less effective if administered before the infections have reached the acme stage. This together with the observation that trypanosomes usually persist sometimes even a increasing in numbers for two to three days after treatment is regarded as supporting the view that immunity reactions play a considerable part in the mechanism of cure and it is in contrast to experience with the treatment of a very acute type of infection e.g. with *T. brucei* where the infection becomes more difficult to cure as it progresses

After non-curative treatment by No 897 and 30 other phenanthridinium compounds tested the duration of the parasite free period on blood examination was generally 9 to 14 days for Strain I and 8 to 11 days for Strain II infections period being apparently independent of (a) the size of dose (b) the stage of infection at the time of treatment and (c) the particular compound used

It was found that in the chronic stage arbitrarily fixed at three to six weeks be acme for Strain I and a few days after acme for Strain II treatment is be early stages less effective than at acme. Such chronic infections are trypano-uated under the designation of chronic in the original mouse from onth salts a chronic strain infections defined as arising when the inoculum is e capable from a mouse in which the infection has become chronic. It was a finding that as many as 28 per cent of 149 mice failed to become any success after inoculation from animals chronically infected with Strain I introduction ons from animals chronically infected with Strain II always produced

s were used. vary the curability of various stages of infection in both Strains I lly described rtng with the most readily cured is as follows —(a) acme (b) early y 32, 30]

(c) a "chronic strain" infection treated at fastigium, and (d) the "chronic stage" in the original mouse. These observations probably have an important bearing on the results under field conditions.

Prophylactic Action.—In contrast to the prolonged protective effect of Suramin and certain benzoxylamino quinoline atvryl compounds against *T. brucei* [BROWNING and GULBRANSEN this *Bulletin* 1933 v. 32, 28] No. 897 exercised only a slight prophylactic effect on *T. congolense* a subcutaneous dose of 1 mgm. protecting against Strain I for two days but not for a longer period.

Oral administration in the form of daily feeding with bread soaked with 1 cc. of 1/1 000 solution, exerted neither prophylactic nor curative action.

Section III—Treatment with other drugs.—A list is given of 46 substituted phenanthridinium compounds examined, all with a benzene ring in the 8-position. General conclusions about this series are as follows:—

The greatest activity against *T. congolense* is exerted by compounds with two amino substituents, situated either both in the phenanthrene nucleus or one in the latter and the other in the benzene nucleus. The actual position of these amino groups does not appear to influence activity but two such groups in the benzene ring in the *m* positions are not associated with activity.

The activity of No. 897 which has an amino group in the phenanthrene and in the benzene nucleus is impaired by the inclusion of a bromine atom in the 3-position.

A single amino group situated in either nucleus increases toxicity and reduces considerably the therapeutic action.

The acetylated derivatives are much better tolerated, but also much less active than the corresponding amino compounds.

An outstanding advantage of 1553 is its relative lack of the irritating effect on the tissues at the site of injection, exhibited by most of the other active compounds of this series.

The phenanthridines corresponding respectively to No. 897 and to one of the other active phenanthridinium compounds, were found to be inactive.

Diamidine series.—The compound 4,4-diamidino dimethyl stilbene considered by FULTON and YORKE [this *Bulletin* 1943 v. 40, 19] to be at least as effective as No. 897 on their strain of *T. congolense* was tested by the author. She found, however, that 1/75 of the tolerated dose of No. 897 has about the same curative action as 1/10 of the tolerated dose of the dimethyl stilbene drug when tested on Strain I at acme. The latter compound appears however to be

just as effective in chronic infections as at acme and it is therefore considered that a possible explanation of Fulton and Yorke's conclusion is that their observations were made on chronic infections.

Quindoline Methochloride (supplied by I.C.I.)—This compound is curative in doses approaching the maximum tolerated (1.3 mgm.) but the severe local reaction at site of injection renders it unsuitable for use. The corresponding hydrochloride is inactive.

Section IV—Treatment of Relapses.—In the case of Strain II which was more exhaustively examined than Strain I under this head, relapsed infections were repeatedly treated by a uniform dose of 0.07 mgm. at each relapse. Fifty six relapsed mice were thus investigated, the greatest number of relapses in any one animal being 29. Cure frequently resulted from these repeated treatments and usually within six retreatments. The chance of cure by the standard dosage was the same in the treatment of relapses as in the treatment, at acme, of original infections (33 per cent). This is contrary to the widely accepted belief, based on observations with infections by other trypanosome species, that cure is more certain by vigorous initial treatment while cure of relapses presents special difficulties. An especially significant interpretation of these findings is that drug-resistance did not develop as a consequence of these

repeated retreatments. Only in two mice out of 47 which received three or more retreatments were there any indications of a slight resistance in so far as relapses failed to respond to further treatment. This is elaborated under Section V.

In the case of Strain I infections successive relapses were treated by 0.01 or 0.013 mgm. Unlike the experience above relapses were in general not as easily cured as the original acute infections. In four mice out of six definite indications of resistance appeared at the third to sixth treatment (in three weeks to two months). The dose was increased to 0.33 mgm. in two of these mice and by the 12th treatment there was no response to this dose. However infections derived from these two mice showed some response to 0.33 mgm. but in most the action disappeared after a few retreatments. Occasionally after only slight responses to several consecutive treatments subsequent treatments did produce a definite effect. On the whole it was concluded that there was strong presumptive evidence that a true drug resistance to No. 897 might be readily developed by this strain but as shown below this proved to be extremely difficult.

Section V. Attempts to develop strains of T. congolense resistant to drug.
No. 897—Strain I was passed through 12 mice in a period of six months during which 20 doses were administered rising from 0.013 mgm. to 0.1 mgm. The strain was then lost. It was considered that there had been no particular development of acquired drug resistance in the ordinary sense the apparent acquisition of the property being explained by the fact that in the course of the treatments a relapse (chronic) strain was developed and such strains have been shown to be less responsive to treatment than the original strain treated at acute (see Section II).

Strain II was passed through six repeatedly treated mice which received altogether 39 doses of 0.07 mgm. and 26 of 0.33 mgm. In several instances which occurred only in the earlier passages there was some degree of resistance to 0.33 mgm. administered at acute but in the subsequent passages this apparent resistance was no longer in evidence.

With both strains further unsuccessful attempts to produce lasting resistance were made by the method designed to leave unimpaired the immunological and serological characters of the parent trypanosomes. This consists in treating the mice at a time when the infection is developing and the trypanosomes are scanty in the blood with a dose which does not affect the course of infection. The parasites are then transferred at acute to a fresh host. With Strain I the attempt involved 16 passages over a period of four months during which the dose was increased from 0.005 mgm. to 0.02 mgm. With Strain II there were 34 passages in 8 months with doses from 0.0013 mgm. to 0.017 mgm.

It was concluded from all this work that true lasting drug resistant strains of *T. congolense* had not been produced and are not easy to produce by these standard methods which are so effective in bringing about resistance to other drugs in other trypanosomes such as *T. brucei*.

Section VI. Immunity Responses after Cure.—This was investigated in considerable detail with very interesting results which cannot all be summarized in a few lines.

With Strain I there is a remarkably solid immunity to reinoculation with homologous acute trypanosomes lasting at least 13 months in mice cured either at acute or in the chronic stage. There is however with very rare exceptions no immunity in such mice to reinoculation with random strains of chronic trypanosomes even if the reinoculation be from the same animal as yielded the original infection.

The results of a considerable number of immunity tests led to the general interpretation that the immunological characters of the trypanosomes undergo progressive change in chronic infections. However by passage of a chronic

infection to a fresh mouse from which the subsequent transfers are made only at the fastigium, the immunological character of the chronic strain may for a time be preserved but after a very variable number of such transfers (less than three or more than 12) the immunological character tends eventually to revert to that of the acute parent type.

Chronic strains are evidently immunologically heterogeneous. Expressed in terms of Ehrlich's receptor theory when an infection of the acute strain is allowed to become chronic additional receptors appear but do not replace the original A type. The receptors may be regarded as becoming progressively A+B A+B+C etc. which on cure gave rise to anti (A+B) anti (A+B+C) etc. Thus a mouse whose immunity depended on anti (A+B) would be immune to trypanosomes with receptors A or A+B (or B) but not to those which contained additional receptors as in A+B+C. The effect of further fastigial passages is to prevent development and accumulation of additional receptors and eventually to lead to their disappearance.

With Strain II in contrast to Strain I mice cured at acute do not manifest a 100 per cent. immunity to reinoculation by homologous acute trypanosomes. The chances of such a reinoculation resulting in infection are about 50 per cent., and bear no relation to the size of dose used to effect cure or to the duration of the period which has elapsed since cure (up to the limit tested, 8 months). Where reinfection does eventuate the incubation period is nearly always about four days longer than in controls this being interpreted by the author as indicating a slight degree of resistance to the homologous strain.

A number of animals which had proved immune were repeatedly reinoculated with acute trypanosomes but the chances of infection remained about 50 per cent. at least for the first few reinoculations with perhaps a tendency to a higher proportion of immunes as the number of reinoculations increased. In similar experiments with Strain I it had been found that cured mice originally infected with acute trypanosomes withstood up to 20 homologous reinoculations.

Cured chronically infected Strain II mice responded to reinoculation with acute parasites in the same manner as cured acute animals (50 per cent. likelihood of immunity) but no immunity was observed in cured acute mice on reinoculation with random chronic parasites. This corresponds with findings in similar experiments with Strain I and it was tentatively concluded that when a Strain II infection becomes chronic, the trypanosomes undergo the same kind of immunological changes as those of Strain I *i.e.* there is an addition to but no replacement of the original receptors.

There is no cross-immunity between the two strains animals cured at acute after infection with acute trypanosomes of Strain I becoming infected on reinoculation with acute parasites of Strain II and *vice versa*. There was however some indication that a history of a cured Strain I infection improves a mouse's chances of developing an immunity to Strain II on cure of a subsequent infection by the latter strain.

Attempts to apply the adhesion reaction of Røckenberg [this *Bulletin* 1917 v 10 56] with a view to detecting immunological differences or identities among the various strains were unsuccessful.

Section II Field Trials of No 897 and No 1553 on T. congolense Infections. These have been as follows —

No 897 — HORNBY EVANS and WILDE (*J. Comp. Path.* 1943 v 53 289) CARMICHAEL and BRILL 1944 (1) [this *Bulletin* 1945 v 42, 259] unpublished communications of du TOIT to the National Institute for Medical Research, 1941 and by MARSHALL to the Department of Scientific and Industrial Research, 1943.

No 1553 —CARMICHAEL and BELL 1944 (2) [this *Bulletin* 1945 v 42, 260]

The author's own results are considered in relation to field trials with the following conclusions —

(1) Favourable reports have appeared from widely separated localities in Tanganyika Uganda and Nigeria although very considerable variation in the tractability of infections in the field might be expected, in view of the fact that the two laboratory strains here described have been shown to differ so much in their reactions to treatment and in related properties

(2) The stage of infection at the time of treatment should be noted, in reports of field trials since this has been shown in mice to be of considerable significance.

(3) The difficulty of producing a drug resistant strain under experimental conditions indicates that No 897 is a valuable drug for use in the field. The resistance reported in relapsed infections [HORNBY *et al* 1943 *loc. cit* CARMICHAEL and BELL 1944 (1) *loc cit*] is probably attributable to the chronicity of the infection rather than to true acquired drug resistance. Thus in the present work the curative dose for a chronic infection may be at least 5 to 10 times that required at acme

(4) The fact that with one of her strains cure at acme is followed by a solid immunity suggests to the author that if such a solid immunity can be demonstrated in the field it may be utilized to protect animals passing through fly belts by previously infecting and then curing them [But natural transmission in the field is very different from blood inoculation of a fastigially propagated strain, and it was only to such inoculations that a solid immunity was demonstrated.] From results obtained with the other strain however the author considers that such protection would not be expected with all strains under field conditions

(5) The author showed that in mice a greater degree of immunity was manifested to laboratory Strain II parasites in the presence of antibodies to Strain I than in animals which had never been infected with the latter. Accordingly it is suggested that a more solid immunity might follow cure of a mixed infection with several strains of *T. congolense* than would occur after infection with a single strain.

E M Lourie

WALLS L. P with a note by C H BROWNING R M CALVER & M W LECKIE
Researches in the Phenanthridine Series. Part VI The Relationship
between Structure and Trypanocidal Properties. *J Chem Soc* 1945
May 294-300

Certain amino-substituted quaternary salts of this series possess trypanocidal properties and the effect of variation in number and position of the substituents has been investigated. An improvement has been effected in the method of ring closure of acyl-o-xenylamines (I→II) and it has been found that the facile preparation of nitro-quaternary salts such as 2,7-dinitro-9-phenyl 10-methyl phenanthridinium chloride (IV $R=R=NO_2$, $R'=H$) followed by reduction offers an alternative and generally preferable route to the trypanocidal types. In order to obtain a similar bromo-substituted compound it has been shown that bromination of 4-nitro-2-acetamidodiphenyl occurs as expected in the 5-position

Activity against *T. congolense* is well maintained in all the diamino-quaternary salts except when both amino-substituents are in the 9-phenyl group. Pronounced action against *T. brucei* is only found in (IV $R=R=NH_2$, $R'=H$) where the amino-groups are in the benzidine position. Acetylation of the amino-groups results always in diminution in activity

UNDERWOOD L. J. Nitritoid Reaction following Tryparsamide Therapy Report of a Case. *Arch. Dermat. & Syph.* 1945 May v 51 No. 5 313-15 [13 refs.]

BRAZZAVILLE [A. E. F.] RAPPORT SUR LE FONCTIONNEMENT TECHNIQUE DE L'INSTITUT PASTEUR EN 1943 [CECCALDI J. Director] 59-85
Surveillance de la maladie du sommeil [Sleeping Sickness.]

Two European missionaries infected at the same time and place were treated at the Pasteur Institute at Brazzaville during 1943 each received about 11 injections of about 1 gm. of moranyl [Bayer 205] during about two months. Both were in the early stage and recovered.

There were 165 new cases among Africans coming from various parts of the territory they were treated with the usual drugs given either alone or in combination. Orsanine (270 F) was considered to be the most effective drug used.

Four hundred and ninety old cases were examined 27 had been diagnosed between 1918 and 1928 (three still infected) and 141 between 1928 and 1938 (14 still infected).

Tests of toxicity of old stocks of atoxyl or trypanyl tryparsamide, and orsanine were made on rabbits, rats and mice atoxyl had altered and was rejected, orsanine had preserved its normal characters, and tryparsamide of French manufacture though slightly altered was more satisfactory than supplies of more recent date of American (SQUIBB) manufacture.

Some observations are given which strongly suggested that reinfection had occurred in some patients after cure
J. F. Corson

WOOD S. F. Additional Notes on the Persistence of *Trypanosoma cruzi* in Dead Insect Vectors. *Bull. S. Calif. Acad. Sci.* Los Angeles, Calif. 1944 v 42 Pt. 3 115-27 [Summary taken from *Rev. Applied Entom.* Ser. B 1945 May v 33 Pt. 5 72-3.]

Details are given of experiments on the persistence of various strains of *Trypanosoma cruzi* in a viable state in nymphs of *Triatoma* spp. after they had died naturally in the laboratory or had been killed or immobilised by exposure to hydrocyanic acid gas. Some treated with the gas survived for many days and could, if stimulated, move legs and antennae, but could not crawl. The longest periods for detection of living stages of the trypanosome after natural death of the bugs were 41 days in *T. protracta* Uhl. three days in *T. protracta* woodi Usinger and 24 days in *T. rubida* Uhl. and the longest periods after death or immobilisation by cyanide were 127 days in *T. protracta* 122 days in *T. rubida* and 16 days in *T. longipes* Barber. The author considers that the persistence of *Trypanosoma cruzi* in dead bugs is of importance in maintaining a large rodent reservoir of infection since rodents acquire infection by feeding on them. They would be particularly likely to notice dying bugs that still moved their antennae or legs.

Some of the bugs in all the cultures used for these experiments were found to be infested by *Erycytes concolor* Hald. This mite occurred most often on *Triatoma rubida* from nests of wood rats [*Neotoma*] in Arizona. No trypanosomes were found in mites from infected bugs.

WOOD S. F. Observations on Vectors of Chagas' Disease in the United States. I. California. *Bull. S. Calif. Acad. Sci.* Los Angeles, Calif. 1942 v 41 Pt. 2, 61-9 [22 refs.] [Summary taken from *Rev. Applied Entom.* Ser. B 1945 May v 33 Pt. 5 72.]

This is the first part of a series of which the second has already been noticed. It includes a review of the papers in which *Trypanosoma cruzi* has been recorded.

in Triatomids in California Arizona Texas and New Mexico a list of the species examined for infection in these States and (with negative results) in Utah showing the numbers of each and the numbers and percentages infected new locality records for infection in *Triatoma protracta* Uhl in California lists of numerous Californian mammals in which infection was not found by blood examination or xenodiagnosis and a discussion of the effects of the bites of Triatomids on man which are severe in some individuals and imperceptible in others In California, *Trypanosoma cruzi* has been found only in *Triatoma protracta* in a single example of *Neotoma fuscipes macrotis* and possibly in a bat.

DAO L LUIS Muertes subitas en la enfermedad de Chagas. [Sudden Death in Chagas's Disease.] *Bol de los Hospitales* Caracas 1944 Nov-Dec. v 43 No 6 303-11 [14 refs] English summary (9 lines)

Two cases are recorded both in men—one aged 39 years the age of the other is not known The former applied for treatment on account of fever shivering sweating and a general tired feeling His heart was enlarged and its action irregular *P vivax* in scarce numbers was found in his blood but no trypanosomes. The xenodiagnostic test was however positive He was treated for the malaria and the fever disappeared Eight months later he suddenly fell dead.

The second patient complained of palpitation which was aggravated on slight exertion His heart was enlarged as was also the liver faecal examination revealed a few ova of *Necator americanus* Xenodiagnosis was positive in this case also About 12 weeks later after a day or two of fever which disappeared without treatment the man was one morning found dead in bed.

The author discusses the possible or rather the probable causes of sudden death He excludes syphilis by the negative Kahn reaction in each case there were no schistosomes to account for the myocarditis hookworms were absent from the first and only scarce in the second patient whereas the positive results of the xenodiagnostic tests proved the existence of Chagas's disease The diffuse myocarditis separation fragmentation and hyaline degeneration of the myocardial fibres are well known in chronic cases of this disease and would readily account for these sudden deaths. Incidentally they add further evidence of the presence of this disease in the State of Anzoátegui Venezuela The author refers to the literature for preceding accounts of sudden deaths of young adults in endemic centres of Chagas's disease

H Harold Scott

LEISHMANIASIS

LOWE J The Early Diagnosis of Kala-Azar *Indian Med Gaz* 1944 Oct v 79 No 10 459-65 3 figs

The importance of the early diagnosis of kala azar is illustrated by the detailed description of five cases in which the most constant finding was the irregularity of the temperature of remittent nature with a relatively rapid pulse and the absence of the marked toxæmia of enteric fever or the headache and pains in the back and limbs so frequently met with in malaria. The absence of toxic symptoms accompanying the early fever is characteristic of kala azar. The only other early findings are a positive complement fixation and the presence of leishmania in sternal puncture material. The complement fixation test is carried out with the W.K.K antigen prepared from acid fast bacilli As regards the discovery of leishmania a search of an hour may be necessary before a parasite can be found in the smears In early cases all the characteristic

features, including the serological and blood changes of well developed kala azar are absent so that diagnosis may be difficult. Nevertheless by careful observation of the general clinical picture and the nature of the fever combined with sternal puncture and the complement fixation test which is often positive in early cases diagnosis should usually be possible within three weeks of onset. One condition however is essential namely that kala azar should be thought of and considered as a possible diagnosis. C. M. Wenyon

STEWART C. D. & PILCHER J. F. American Leishmaniasis. Report of an Autochthonous Case. *Arch Dermat & Syph* 1945 Feb v 51 No 2, 124-8 2 figs [Refs in footnotes]

American leishmaniasis (muco-cutaneous leishmaniasis) a common disease in S. America is of rare occurrence in the United States. Only three cases have been reported in the literature and of these only one has been regarded as autochthonous. This was a case reported by BENEDEK [this Bulletin 1940 v 37 778] Fox (*Arch Dermat & Syph* 1941 v 43 1093) however expressed a doubt, as the patient had spent four years in Poland fifteen years prior to the development of mucocutaneous lesions of the nose. Fox stated that if the disease were really American leishmaniasis it must have been contracted in Poland [a conclusion which seems unjustifiable as no form of leishmaniasis has ever been reported from that country]. However this may be there appears to be considerable doubt about the diagnosis in Benedek's case as pointed out by the reviewer. The case reported in the present paper was in a boy six years of age who had never been more than 60 miles from his birthplace near Alice in Texas. He first developed a papule on the dorsum of the left foot. This gradually enlarged and ulcerated, while similar papules and ulcers developed on the right foot, knee and buttock. There were few subjective symptoms, though a generalized lymphadenopathy was noted. In sections of tissue removed from the ulcer on the right foot bodies were seen within cells or free in the tissue spaces. These were identified as leishmania by the authors and other observers. About a year later the cutaneous lesions had healed but superficial ulceration on both sides of the anterior part of the nasal septum was discovered. The generalized lymphadenopathy persisted. In spite of the fact that leishmania were not found in the nasal ulcers the authors state that they have no doubt that the nasal lesions represent the beginning of the tertiary stage of American leishmaniasis. [It is unfortunate that leishmania were not found in Giemsa-stained smears of any of the lesions for the identification of these parasites in sections is always open to question unless made by an observer who has had extensive experience of these particular organisms. The microphotograph illustrating the paper is a good one but though suggestive of leishmania, it is not absolutely convincing.] C. M. Wenyon

PESSÓA, S. B. & VILLELA, F. Nota sobre tratamento da leishmaniose tegumentar americana pelo antimon-ditoxim [Treatment of Cutaneous and Muco-cutaneous Leishmaniasis with "Antimon-ditoxin"] *Brasil Medico* 1944 Nov 18 & 25 v 58 Nos 47 & 48 442-3

The authors give an account of their experience in the treatment of cutaneous and muco-cutaneous leishmaniasis with antimon-ditoxin. This is a preparation issued by Wulff of Berlin. It is similar to auro-ditoxin and is put up in ampoules to be dissolved in the solvent supplied. The makers advise the administration by intramuscular injection a dose to be given every two days, commencing with 0.05 gramme. The second and third doses are 0.1 and 0.2 gm. respectively. The 0.2 dose is continued for a further 8 or 10 injections. The

authors found that in this dosage there were no signs of toxicity so in some cases they continued the 0.2 gm. dose for 30 injections. In certain resistant cases 0.3 gm. was used. It was evident that the drug had a curative action on several cases of naso-pharyngeal involvement some of which cleared up entirely. Though the drug is evidently superior to tartar emetic and Fouadin some relapses occurred. In view of its low toxicity the authors propose using the still larger doses of 0.3 to 0.5 gramme

C. M. Wenyon

FEVERS OF THE TYPHUS GROUP

BLANC G. MARTIN L. A. BALTAZARD M. Etude du comportement des virus exanthématiques chez divers ectoparasites. [Study of the Behaviour of the Typhus Rickettsiae in various Ectoparasites.] I Comportement du virus du typhus murin chez le pou de l'âne *Haematopinus asini* [BLANC MARTIN & BALTAZARD] *Arch Inst Pasteur du Maroc* 1944 Oct v 2 No 4 578-85 II Comportement du virus du typhus épidémique chez les puces *Xenopsylla cheopis* et *Pulex irritans* [BLANC & BALTAZARD] *Ibid* 586-601 III Comportement des virus de la fièvre boutonneuse et de la fièvre pourprée chez les puces *Xenopsylla cheopis* et *Ctenocephalus canis* [BLANC & BALTAZARD] *Ibid* 602-10 [Bibliography]

In the experimental work dealt with in this abstract an insect is regarded as being a potential vector when the following conditions are complied with — (1) The insect is infected by a single meal (2) The insect should remain infected for life (3) The virus should multiply in the body of the insect (4) The virus must be demonstrable in the faeces of the insect and must survive in the dried faeces.

I Behaviour of Murine-Typhus Rickettsiae in the Ass-Louse *Haematopinus asini* [see this *Bulletin* 1940 v 37 262]

The above conditions were fulfilled in the case of lice collected from two asses which had received massive intravenous injections of murine rickettsiae. The lice were first found infected 10 days after the inoculation of the hosts. Lice collected during the febrile stage of the illness of the asses were not infected.

II Behaviour of Epidemic Typhus Rickettsiae in the Fleas *Xenopsylla cheopis* and *Pulex irritans*

X. cheopis fed on a single occasion on guineapigs infected with epidemic typhus also complied with the above conditions. They remained infected for the rest of their lives which were not shortened by the infection. Further experiments confirmed the findings of DYER and others that the flea does not transmit infection by its bite. Three out of five monkeys became infected after the application of infected flea faeces to the conjunctiva or to the nasal and buccal mucosae.

P. irritans also complied with the prescribed conditions and can be regarded as a potential vector of epidemic typhus but it is difficult to rear and does not feed readily on guineapigs.

III Behaviour of the Rickettsiae of Boutonneuse Fever and Rocky Mountain Spotted Fever in *Xenopsylla cheopis* and *Ctenocephalus canis*

By a series of experiments in which white rats and guineapigs were used it was found that the rickettsiae of boutonneuse and Rocky Mountain fevers survived in the bodies of the above fleas but did not multiply in them and were not passed out in the faeces. This is a new observation. The other two—I and II—have already been published.

John H. D. Megaw

BLANC G & BALTARARD M. Recherches sur l'immunité dans les maladies évanthématiques humaines. [Investigations into the Immunity conferred by Human Typhus Fevers.] I Immunité conférée par l'infection apparente. *Arch. Inst. Pasteur du Maroc*. 1944 Oct. v 2, No. 4 611-24. II Immunité conférée par l'infection inapparente ou l'infection "atténuée. *Ibid* 625-32. III Qualité de l'immunité. Réinfection inapparente. *Ibid* 633-50. IV Immunité générale et immunité locale. *Ibid* 651-5 [Bibliography]

The work described in this memoir was carried out in Morocco between 1933 and 1942 some of the findings have already been published.

I. Immunity Conferred by Apparent Infection.

Experiments were carried out in which five strains of murine rickettsiae, seven strains of epidemic, nine strains of boutonneuse, and one strain of Rocky Mountain spotted fever rickettsiae were used. In the course of the investigation 683 guinea-pigs, 91 human beings and 36 monkeys were employed.

It was found that a frank attack either of murine or epidemic typhus caused complete and lasting immunity against both murine and epidemic infection. In the case of one human being the immunity was tested after 5½ years.

A corresponding degree of immunity was conferred against both boutonneuse and Rocky Mountain infection by a frank attack of either of these diseases.

All the strains of each of the rickettsiae were found to be identical in their pathogenic and antigenic powers, and, especially in the case of murine typhus, there was no difference in virulence or immunizing powers, although the strains came from three different countries and included one from Mexico.

II Immunity Conferred by Inapparent or "Attenuated" Infection

In a large series of experiments it was found that certain animals and human beings which had shown no obvious reaction to a virulent experimental infection were afterwards (up to five years in one case) found resistant to massive doses of infection, and so could be assumed to have had an inapparent infection in the first instance.

Just as bile-treated living vaccine made from endemic typhus rickettsiae protects against both endemic and epidemic infection, so also living vaccine prepared from boutonneuse rickettsiae was found to protect 34 guinea-pigs and four monkeys against both boutonneuse fever and Rocky Mountain spotted fever although the response to the vaccine in the case of the guinea-pigs had been inapparent and in the case of the monkeys had been attenuated. The authors insist that the only proof of the occurrence of an inapparent infection is the production of immunity against the organism concerned when this immunity does not develop the inoculation must be regarded as having failed. The occurrence of a slight febrile response is not evidence that infection has occurred workers with murine and boutonneuse rickettsiae know from experience that the result of intraperitoneal inoculation of guinea-pigs nearly always is either apparent infection or a failure to infect they also know that the recovery of the rickettsiae from the blood of the animals is very difficult even when the infection is intense when the infection is inapparent it is almost impossible. The authors have however succeeded in isolating the virus from guinea-pigs inoculated intradermally with bile-treated murine vaccine the method was one of xenodiagnostics the infected animals were kept in a receptacle containing large numbers of laboratory-bred fleas, from which suspensions were made after 30 days. They conclude that when a person or animal is found susceptible after inoculation with attenuated live rickettsiae, there must have been a failure to produce infection.

III The Quality of the Immunity Inapparent Reinfection.

Numerous attempts were made to demonstrate the occurrence of inapparent infection in animals that had recovered from attacks of murine, epidemic

and Rocky Mountain fever dating from one and a half to seventeen months previous to the experiments. Out of a very large series success was obtained in only one case in which a guinea pig became infected with Rocky Mountain spotted fever 14½ months after recovery from an inapparent attack of boutonneuse fever. Inapparent reinfection must therefore be very rare and animal reservoirs of infection must be infective to the vectors only during the brief periods while they are suffering from their first attacks.

In the tick borne typhus fevers hereditary transmission in the ticks (transmission through the egg would be a more accurate expression) readily explains the persistence of infection but in murine and epidemic typhus another explanation must be sought.

IV General and Local Immunity

Various experiments hitherto unpublished are described which confirm the observations by GIROUD and the authors that the sites of intradermal and intraorbital inoculations with typhus rickettsiae are less sensitive to reinoculations than other corresponding sites.

John W D Megaw

BLANC G E BALTAZARD M Recherches sur le mode de transmission du typhus [Investigation of the Mode of Transmission of Typhus Fever]

I Non transmission du typhus exanthématique par piqûres de poux infectés *Arch Inst Pasteur du Maroc* 1944 Oct. v 2 No 4 636-7

II Le réservoir de virus naturel des typhus les déjections d ectoparasites infectés *Ibid* 658-73 [Bibliography]

I Non-transmission of Typhus Fever by the Bites of Infected Lice

This note has already been published (*Bull Acad Véd* 1942 v 126 444) under the same title.

Eight human volunteers were bitten by a large number (about 140 each) of infected lice kept in a tube whose mouth covered by bolting silk was kept upwards while the lice were feeding so that there was no possibility of contamination of the skin by the droppings of the insects. No infection resulted the lice were later proved to be infected and the volunteers were afterwards shown to be susceptible to murine typhus.

II The Natural Reservoir of the Typhus Rickettsiae is infected Faeces of the Ectoparasites.

In this paper the authors have brought together the reports of various investigations already published by them in separate papers from 1937 to 1942.

The method of collecting the faeces of infected fleas is described. Stress is laid on the uniform virulence and the indefinitely prolonged keeping properties of the dry faeces.

John W D Megaw

BLANC G & BALTAZARD M Transmission et conservation naturelles des typhus Immunité Epidémiologie Prophylaxie [The Natural Transmission and Maintenance of Infection of the Typhus Fevers. Immunity Epidemiology Prophylaxis.] *Arch Inst Pasteur du Maroc* 1944 Oct. v 2 No 4 674-715 [157 refs] [Bibliography]

In this note hitherto unpublished the authors discuss the subjects mentioned in the title. They again insist that none of the typhus rickettsiae can undergo mutation by passage through invertebrate vectors although the rickettsiae form groups the members of each of which show a considerable range of adaptability to different vectors. The groups recognized by the authors are (a) epidemic and murine rickettsiae each of which is experimentally transmissible both by various lice and various fleas and (b) the tick borne typhus rickettsiae each of which is transmissible by a considerable number of species of ixodid ticks. The rickettsiae belonging to each of these groups are not transmissible

by the vectors which transmit those of the other group. The authors surprisingly state that the various rickettsiae of the river fever in the East Indies, China and Japan ought to be included among the rickettsiae of the tick borne group. This is the only mention that is made of mite-borne typhus fever.

The authors admit that murine rickettsiae may exceptionally be transmitted in natural conditions from man to man by lice and so give rise to small human epidemics but they argue that if this should ever happen it could only be in louse-infested communities and that a benign infection would be caused which would help to stamp out epidemic typhus in the affected area. In a chronological review of the question of transmission, the authors in the same number of the *Archives de l'Institut Pasteur du Maroc* state that the mystery of tabardillo in Mexico has arisen because of the coexistence of murine and epidemic rickettsiae in the same locality and that contrary to an erroneous statement made by themselves there is no evidence that the human louse has ever been found naturally infected by murine strains.

In discussing the maintenance of typhus infection during inter-epidemic periods the authors refuse to admit that inapparent attacks play any important part though during actual epidemics such attacks help to maintain infection among lice. Occasional sporadic attacks during inter-epidemic periods are believed to be caused by dried infected faeces adhering to the clothing of persons who have been attacked during epidemics. The sporadic attacks are not usually highly infectious but for unexplained reasons one of them may be highly virulent and so give rise to a fresh epidemic. Infected faeces of lice are quickly inactivated by moisture so that the mere washing of patients' clothing is a valuable measure of control. Sterilization of the clothing by steam under pressure, is however more reliable because it destroys the lice as well as the rickettsiae. Louse control, by itself is inadequate.

The nature of the immunity in typhus fevers is discussed at some length. The authors assume that so long as antibodies can be detected in the serum the rickettsiae still persist in the internal organs and immunity remains complete. This condition may last for several years. After the disappearance of the antibodies and the rickettsiae immunity becomes partial so that inapparent attacks may occur. The authors also believe that attacks may occur in which the endothelial cells are not invaded, so that the infection is purely humoral. This condition may exist in healthy carriers of infection and in inapparent reinfections and it would not give rise to lasting immunity such as is produced by the presence of the rickettsiae in the cells. The immunity produced by killed vaccines is believed to be of this humoral and therefore short-lived type.

[It has been possible to mention only a few of the findings and expressions of opinion recorded by the authors in the collected papers dealt with in this and the three preceding abstracts. These papers constitute a comprehensive report of the vast amount of experimental work carried out by them during the past few years.]

JOHN W. D. MEGAW

CASASEDA, M. RUIZ. Differentiation of Typhus Strains by Slide-Agglutination Tests. *J. Immunology* 1945 Mar v 60 No 3 179-83

A rickettsia-agglutination slide test has been used by the author to show that antigenic differences exist between classic and murine typhus. The rickettsia suspensions were made from the lungs of mice infected intranasally by murine and classic strains and were standardized by slide-agglutination tests of sera of guinea-pigs or rabbits convalescent from murine and classic

infections. Equal drops of the suspensions and of sera diluted 1-5 to 1-80 were mixed on the slides which were kept in gentle movement the readings were made after 1-3 minutes with a pocket lens. In all the examples given in the paper the agglutinations with the homologous sera were always at titres at least four times as high as those with the heterologous sera.

In applying the test to human sera dilutions ranging from 1-20 to 1-640 were used inactivation of the serum did not affect the result. A loop of 4 mm outside diameter was made with No 24 wire with this single drops of diluted sera and of suspensions were mixed on the slides which were placed in large Petri dishes each containing a piece of wet cotton and kept moving for 5-10 minutes.

In a table the results obtained by complement fixation and slide test applied to the same sera are compared. In the following three examples the first serum was from a patient convalescent from proved murine typhus the other two were from patients living in an area where only murine typhus had been known to occur.

Day of Disease	Weil-Felix titre	Complement fixation titre		Slide-agglutination titre	
		Classic	Murine	Classic	Murine
Convalescence	640	20	160	160	1 280
12th	640	160	640	40	160
12th	640	0	160	80	640

The Weil-Felix titres shown above were the highest tested.

In most of the other 10 cases in which the identification of the type of the disease was based solely on the tests the responses were equally clear-cut but in one of the sera the complement fixation titre was the same (1-320) with both murine and classic antigen whereas in the slide test the titre with murine rickettsiae was 1-160 and that with classic rickettsiae was 1-640. In another case the titres of both tests were only twice as high with classic antigens as with murine. In still another case there was a great discrepancy between the results with the two tests the fixation titre was 1-160 with classic antigen and 0 with murine yet the corresponding titres with the slide test were 1-320 and 1-160.

There were altogether four cases among the 13 in the present series in which the agglutination titres with the presumably homologous human sera were only twice as high as those with the presumably heterologous sera and some serologists are likely to doubt whether this difference is significant in a test of this kind. With the complement fixation test the differences in titre were much more pronounced though exceptionally in one case the titres with classic and murine antigen were the same and in another the classic titre was 1-160 and the murine 1-80.

In two cases the tests were carried out as early as the 8th day in both of these the complement fixation test was still completely negative whereas the slide-agglutination tests were positive at a titre of 1-80 in each case. Later reactions (16th and 23rd days respectively) were strongly positive with both tests.

In the discussion of the results the author states that the reliability of the test in the differential diagnosis of classic and murine typhus is open to the same criticism as applies to the complement fixation test.

He also points out that the sera of rabbits and guinea-pigs infected with murine rickettsiae show cross agglutination with classic rickettsiae to a higher

degree than is the case when the animals are infected with classic rickettsiae and the sera are tested against murine rickettsiae. He suggests that there are probably more classic elements in the murine antigen than murine elements in the classic antigen. He regards this finding as being in keeping with the evidence produced by himself that murine vaccines give greater cross protection than classic vaccines.

John W D McGraw

SILVA-GOYTIA, R. Fijación de complemento con sueros de enfermos de tifo exantemático [Complement Fixation in Sera of Typhus Patients.] *Rev Inst Salubridad y Enfermedades Trop Mexico* 1944 Dec. v 5 No. 4 241-5 English summary (8 lines)

The author employed the technique described by Plotz except that the antigen used was a preparation of animal-lung rickettsiae. The results are not given in detail, but they are stated to have been generally comparable with those obtained by Plotz who examined specimens of the same sera.

Using murine and classic antigens, the author tested sera from 300 cases of typhus most of the subjects had been attacked in Mexico City between 1936 and 1944. Of the sera, 229 reacted more strongly with the classic antigen and 31 with the murine. In the remaining 30 the titres were much the same with both antigens. These results are regarded as confirming the opinion of CASTAÑEDA and SILVA that the typhus of Mexico is predominantly classic in type [see this Bulletin 1940 v 37 259].

John W D McGraw

GOLDEN, A. Morbid Anatomy of Typhus as seen in a recent Guatemalan Epidemic. Observations on the Disease. *Arch Pathology* 1945 Apr v 39 No 4 226-31 7 figs

The abundant material investigated by the author was obtained from the bodies of ten persons who had died of epidemic typhus in a mental diseases hospital in Guatemala. The paper is illustrated by ten good photomicrographs.

Interstitial myocarditis ranging from slight to severe, and patchy in its distribution was seen in every case. The muscle fibres of the affected patches were separated from each other by oedema and infiltrations of mononuclear cells with a few polymorphonuclears. Occasionally necrosis of the muscle fibres was seen. No close relationship could be observed between the patches of myocarditis and vascular lesions.

Throughout the central nervous system the lesions were intimately related to small arteries and arterioles affected by endothelial hyperplasia and proliferation and often surrounded by one or more layers of glial cells. Vacuolation of the nervous tissue was common, so also were perivascular haemorrhages and zones of necrosis. Frankel's nodules were found in large numbers, these contained varying numbers of glia cells and their relationship to the affected blood vessels was frequently obvious. In the leptomeninges there were patches of round-cell meningitis. The pia-arachnoid meshes were oedematous and were infiltrated by lymphocytes, plasma cells and large mononuclear phagocytes.

Some of the gland cells of the adrenals were necrosed. In the spleen haemorrhagic foci or zones of necrosis, sometimes both of these, were seen. Hypoplasmia of the liver cells was not uncommon, occasionally also there were zones of necrosis in the liver. The exanthematic plaques in the skin showed vascular lesions similar to those seen in the central nervous system. Some of the renal tubules contained yellow or brown homogeneous casts of haemic origin.

and sometimes red blood casts were seen. Occasionally also there was subacute interstitial nephritis but no vascular lesions were found. In the testes the characteristic vasculitis was conspicuous. It was often accompanied by thrombosis and perivascular round-cell infiltration.

The author regards the condition of haemoglobinuric nephrosis as being similar to that occurring in cases of extensive burns or of the "crush syndrome."

The absence of any obvious association between the lesions and vascular changes was a striking feature of sections of the myocardium, meninges, adrenals, kidneys, liver and spleen.

The author states that one can only speculate on the after-effects that would result from the necrotic lesions of the central nervous system when they occur in patients who survive. The healing of such lesions could only be by neural scar formation.

John W. D. Megaw

ROTH V. E. Reactions to Typhus Vaccine. *Bull. U.S. Army Med. Dept.* 1945 May No. 88: 111-13.

In a footnote to this article the editor of the journal in which it appears states that millions of doses of egg yolk vaccine have been given and that the number of reactions has been negligible. Desensitization is not recommended.

Of the 32 reactions seen by the author 23 were of the usual type with moderate fever, chills and malaise. The remaining 9 were allergic with gastrointestinal, urticarial or asthmatic symptoms or with combinations of these. The onset was explosive with eosinophilia. There was no fever.

Cox, who was consulted, regarded the allergic reactions as due to residual egg antigen contained in the vaccine and stated that the quantity of this residue had recently been greatly reduced.

Four of the patients were definitely allergic to eggs. Three others gave a history of different forms of allergy.

John W. D. Megaw

STOWMAN R. Typhus during the War. *Epidemiological Information Bull.* (UNRRA Health Division) Washington D.C. 1945 Apr. 30 v. 1 No. 7: 289-310.

BLANC G. & BALTAZARD M. Revue chronologique des recherches expérimentales sur la transmission et la conservation naturelles des typhus. [Chronological Review of Experimental Research on the Transmission of Typhus and the National Conservation of the Rickettsiae.] *Arch. Inst. Pasteur du Maroc* 1944 Oct. v. 2, No. 4: 535-77.

LIC W. T. Studies on the Murine Origin of Typhus Epidemics in North China. 3. Isolation of Murine Typhus Rickettsiae from Rats, Rat Fleas and Body-Lice of Patients during an Epidemic in a Poor House. *Chinese Med. J.* Washington D.C. 1944 Apr.-June v. 62 No. 2: 119-39. [32 refs.]

The author regards the present investigation as completing the evidence of the murine origin of epidemics of typhus fever in Peiping where he had already investigated the problem and had found reason to believe that murine rickettsiae could be transmitted from man to man by lice. [See this *Bulletin* 1942 v. 39: 143 and 144.]

In a poorhouse with 350 inmates living in overcrowded and insanitary conditions the disease was detected in February, 1941. The numbers of cases in that and the following months were 6, 3, 19, 11, 2 and 4. There were 6 deaths, 4 of which were in children, presumably many of the adults had been immunized by previous attacks.

Murine strains of rickettsiae were isolated from—two rats, two lots of rat fleas (one was *Ceratophyllus anisus*, the other *Xenopsylla cheopis*)—three

[September 1941]

lots of rat mites (*Liponyssus bacoti*) and three lots of human lice from the clothing of patients. No evidence of infection could be found in human fleas (*Pulex irritans*) or in bedbugs. There was doubtful evidence of infection in unidentified ticks collected from some of the rats. No lice were found on any of the rats that were examined.

[The author's findings do not seem to provide final evidence that the attacks were louse-borne. The outbreak occurred during the season of greatest prevalence of rat fleas this is stated to have been February to September.]

John W. D. Meyer
U.S. Army Med Dept 1945 Maf No 88 85-7

Morehead J. F. Scrub Typhus from an Epidemiological Viewpoint. Bull
This note deals with the epidemiological conditions observed during an outbreak of scrub typhus among the staff of a large hospital which had just been established on a South-Pacific island. The buildings occupied an area of one-half mile square on a plain between mountain and sea and surrounded by jungle. The area was covered by *Awai* grass six feet high. There were 71 cases, the highest incidence was among the mess personnel who were most exposed to contact with rats. Infection in several instances was traced to small sharply defined areas several cases occurred in a unit encamped on a site less than 100 yards in diameter. The incidence dropped sharply after the adoption of the following measures of control—(1) trapping rats (2) cutting and burning of *Awai* grass by native labour (3) spreading sand over the hospital area (4) wearing leggings (5) the liberal use of the repellents dimethyl phthalate and 612. The infection was exceptionally virulent and a large proportion of the staff was attacked.

Walsh N. An Epidemic of Tick Typhus in East Africa. East African Med J
1945 Jan v 22 No 1 11-14

During the period May-August 1944 30 Italian prisoners of war were attacked by tick typhus in East Africa. None of the patients became seriously ill. In every case there was a history of one or more bites by ticks which infested the tall grass of the camp site and the numerous dogs in the camp. A painless local lesion was found in every case but this was never at a site from which the patient had removed a tick. The lesion is described as lenticular about three quarters by half an inch. It is surrounded by a narrow zone of inflammation and congestion. The centre became pale after a few days and developed into a small papule which later became a central eschar. The discrete morbilliform rash was most abundant on the chest and abdomen. The legs were much less affected. The face and scalp were invaded in five cases. The soles in one but the palms were not affected.

Early tenderness and enlargement of the inguinal glands occurred in all the cases. Some other gland groups most often the cervical was affected later. The onset was rapid. The temperature fell to normal with the appearance of the rash about the 5th day. The temperature gradually rose again and remained high for 4-7 days. The fall was by lysis. The chief symptoms were frontal headache, mœnum, depression and anxiety. Leucopenia was usual in three patients there was mild leucocytosis. In 23 cases the Weil-Felix reaction was negative. All the seven positive sera agglutinated Proteus OXA at titres of 1:25 or 1:50. Two also agglutinated *Pr* OX19 (1:25 and 1:50) and one agglutinated *Pr* OXA at a titre of 1:25.

John W. D. Meyer

TOVAR R. M. Rickettsioses exantematicas transmitidas por garrapata en America [Exanthematous Rickettsioses transmitted by Ticks in America. (Tick-Borne Typhus Fevers)] *Medicina Mexico* 1945 Mar 10 & 25 v 25 Nos 479 and 480 65-85 89-96 9 figs [71 refs.]

In this thesis the author gives a succinct and fully-documented account of all the most important work that has been done in the American Continent on tick borne typhus fever. The bibliography contains 71 references. Some of the author's conclusions are of interest. He states that yolk-sac cultures cannot be obtained in sufficient strength and purity for their successful use in the preparation of vaccines against tick-borne typhus or in carrying out the complement fixation test. He favours the use of a vaccine prepared from infected ticks.

He states that tick-borne typhus is regarded as the most widely distributed rickettsial infection in America and that it probably occurs in many places where it has not yet been detected. The virulence of the infection is exceedingly variable, diagnosis is often very difficult and may be impossible without a complete laboratory investigation.

The disease may often be missed because a positive Weil Felix reaction is commonly regarded as being diagnostic of endemic typhus and the possible occurrence of the tick borne disease is not taken into consideration.

Tick-borne typhus closely simulates flea-borne typhus in its clinical pathological and immunological characters so that a unitary aetiology of these two diseases is suggested.

John W. D. Megaw

MARIOTTE C. O. BUSTAMANTE M. E. & VARELA, G. Hallazgo del *Rhipicephalus sanguineus* latreille infectado naturalmente con fiebre Manchada de las Montañas Rocosas en Sonora (Mexico) [Specimens of *Rhipicephalus sanguineus* found naturally infected with Rocky Mountain Spotted Fever in Sonora (Mexico)] *Rev. Inst. Salubridad y Enfermedades Trop. Mexico* 1944 Dec v 5 No 4 297-300 1 graph [11 refs.] English summary (2 lines)

Rickettsiae isolated from a batch of *Rhipicephalus sanguineus* from a dog in Chimal caused scrotal reaction and death in guineapigs.

Guineapigs recovered from exanthematic typhus were susceptible to the strain, but other guineapigs that had survived infection by Rocky Mountain spotted fever were immune.

John W. D. Megaw

YELLOW FEVER.

COLONIAL OFFICE. Fourth Interim Report (being a Revised Version with certain Additions and Appendices, of the Third Interim Report) of the Inter-Departmental Committee on Yellow Fever Control. 1944 December 18 pp. [Miscellaneous No 503B.]

[Permission to publish this review has been obtained from the Controller of His Majesty's Stationery Office.]

The dislocation of the activities of the Office International d'Hygiène Publique in Paris in the summer of 1940 together with the extension of the theatres of war and the rapid opening of the new routes of communication called for the formation of some body to suggest further means of control of yellow fever in Africa. This matter was brought to a head by the severe outbreak of yellow fever which occurred in the Anglo-Egyptian Sudan in 1940-41. As a result of co-operation between the Colonial Office and the War Department in London an Inter-Departmental Committee was set up consisting of representatives of

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the Armed Forces the Government Departments, and the regions of the Commonwealth which were concerned. Individuals who have been actively engaged in Yellow Fever research in England and America were consulted at various times on particular aspects of the problems as they arose.

A number of recommendations have been made concerning the most important measures of control that should be encouraged.

Strict control of *Aedes aegypti* and other potential mosquito vectors of yellow fever should be carried out particularly in the vicinity of aerodromes, warships and ports and at stopping places along transport routes.

Anti-*Aedes* services should be maintained permanently with adequately trained staff in order to keep the *Aedes* Index at not more than 1 per cent at any time of the year.

The necessity for early detection and correct diagnosis of the disease followed by notification and isolation of cases should be stressed to all medical and other personnel likely to be concerned. Because of the difficulty of clinical differentiation between mild cases of yellow fever and other febrile conditions it is recommended that in endemic areas samples of fever in which no obvious cause is detected. Blood should be collected in the acute stage and again three weeks later in all suspected cases in which recovery takes place. If on the other hand the patient dies within ten days from the onset of the illness a specimen of liver tissue should be taken and sent to the nearest laboratory that undertakes the histological diagnosis of yellow fever. It is recommended that viscerotomy services be maintained in endemic areas as the surest method of detecting yellow fever.

All travellers by land sea and air within or passing through the endemic areas as well as all non-Africans living in the areas should be inoculated against yellow fever with a potent vaccine. Supplies of vaccine are maintained in England, U.S.A. South America and West and East Africa. Persons inoculated with a normal immunizing dose of a potent vaccine are protected on and after the tenth day calculated from the day of inoculation. [The scientific evidence on which this statement is based is included in an Appendix to the report.] Inoculation is accepted as providing protection for four years. An attack of yellow fever confers lifelong immunity and persons who have recovered from the disease need not be inoculated or subjected to quarantine. The committee also recommend that guards and regular staff of aerodromes should be immunized and that casual labour employed on aerodromes should be immunized to the fullest extent possible.

Any individual who is travelling from yellow fever endemic areas to those where yellow fever does not exist but in which there may be conditions which permit of its development and who does not carry a valid inoculation certificate should, at the first recognized stopping place in the latter areas be quarantined in properly screened quarters until six days have elapsed from the date of leaving the endemic area. Any suspected individual who shows a rise of temperature on or before the sixth day should be kept in quarantine until the cause is determined.

[A valid inoculation certificate is one certifying—

- (i) That the bearer has been inoculated for the first time more than ten days and less than four years previously or
- (ii) That he has been re-inoculated within the past four years or
- (iii) That he has recovered from an attack of yellow fever and that his blood contains immune bodies against yellow fever as proved by a test carried out by an Institute regularly carrying out biological tests for yellow fever.]

The Committee consider that insufficient attention has been directed to the effective disinsectization of all aircraft moving within or through endemic areas. The insecticide should be applied by hand spray connected to a supply of air under pressure or by apparatus of the Aerosol bomb type. Disinsectization should be carried out on departure of the aircraft from the last airport in an endemic area and on its arrival at the first airport of call in a non-endemic area.

A building free zone of 440 yards should be maintained around the perimeter of all aerodromes. Guards may be housed within the boundaries provided they are immunized but casual labour should not live within the area. The term *Anti-amaryl* should no longer be applied to any aerodrome all aerodromes must be considered potentially infected if they are in an endemic area.

F O MacCallum

AFRIQUE OCCIDENTALE FRANÇAISE RAPPORT SUR LE FONCTIONNEMENT
TECHNIQUE DE L'INSTITUT PASTEUR EN 1943 [DURIEUX C.] 59-70
Service de la fièvre jaune. [Yellow Fever Service]

The yellow fever virus used for vaccination was a French strain which was isolated at Dakar in 1927 and had sustained 257 passages no further animal passages were made during 1943 as it was thought better to keep the dried virulent mouse brain in the refrigerator and so safeguard the success of the inoculations needed for the preparation of the vaccine. During the year 4 097 000 doses of dried vaccine were made and 41,960 ampoules of 2 cc of gum arabic solution for the suspension of the vaccine at the time of use. Altogether 2,953,349 persons were vaccinated 10,270 being of white race. The vaccine was used either alone or mixed with smallpox vaccine and vaccination was done by scarification of the skin. By the end of the year 1943 at least half the population of French West Africa had been vaccinated.

In 1943 as in preceding years it has been very difficult owing to shortage of suitable food to maintain a supply of white mice for protection tests and this has frequently hindered the work. The need for an animal breeding station was urgent and 37 hectares (about 90 acres) of land were acquired about 16 miles from Dakar it was hoped to begin the construction of four animal houses stores and a house for the European manager early in 1944.

Protection tests—During 1943 the blood serum of 67 persons was tested 45 to test the effectiveness of vaccination and 22 for the diagnosis of yellow fever of the former 44 had received the vaccine of the Dakar Institute five subcutaneously and 39 by scarification using Laugret's egg yolk method. The five former persons had been vaccinated six years eight years (2) and nine years (2) before the test all the sera were strongly positive. In a table showing all the tests made by this method it is seen that 85 per cent of 713 sera were positive [44] were tested less than one year after vaccination and 107 at 1-2 years] and 85.9 per cent were strongly positive of 29 vaccinated 5-9 years before 26 had positive and 25 strongly positive sera.

The results of scarification were equally good 37 of the 39 [36 tests within two years after vaccination] being positive and 35 strongly positive. A table shows that of a total of 2 403 persons vaccinated by scarification [2,390 tested within two years after vaccination] 95.8 per cent were positive and 83.8 per cent strongly positive. [The number of mice used in the tests is not given.]

Diagnostic tests—Nineteen of the 22 sera were taken during the course of an illness or immediately afterwards six gave a strongly positive result thus excluding a diagnosis of yellow fever one was weakly positive and was probably a case of a late reaction to vaccination and the other 12 were negative. Two of these 12 persons however had strongly positive sera after recovery thus confirming the diagnosis of yellow fever and in three fatal cases the diagnosis of

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yellow fever was confirmed after death in two and by isolation of the virus in the third. The other seven (natives) remained doubtful as they became unavailable for testing.

Samples of blood from 14 sick persons were inoculated into white mice four of the patients were found to have yellow fever by post-mortem examination or by serum tests but virus was isolated from one only. Examination of the livers of 32 people showed that 10 had died of yellow fever.

Yellow fever in French West Africa—Twelve cases of yellow fever (eight in Europeans and four in Africans) were diagnosed during the year 10 being fatal three were in Senegal eight in Guinea and one in the Ivory Coast. As in the preceding years most of the cases seemed to be related to a reservoir in wild animals since infections occurred in persons living isolated in the bush or in very sparsely populated places. Only one of the patients a European, had been vaccinated against yellow fever and his serum had never been tested but the vaccine used had been proved to be active by tests on others who were vaccinated at the same time and place. It is thought that this patient either could not develop antibodies or that they had disappeared very quickly. The author states that some persons if not watched, will remove the vaccine before it has had time to enter the skin.

J F Corson

PLAGUE.

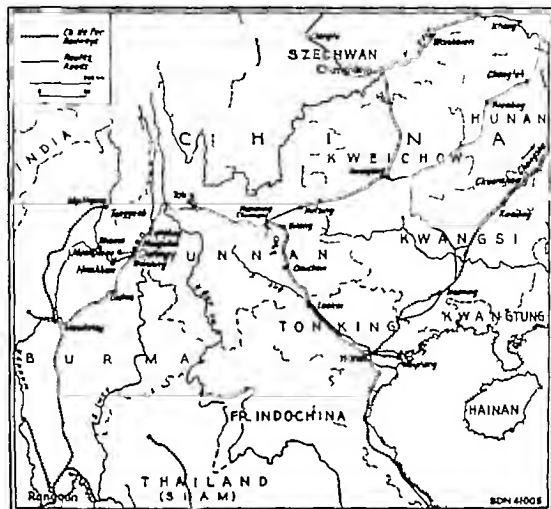
EPIDEMIOLOGICAL INFORMATION BULL. (UNRRA Health Division)
Washington D C 1945 Feb 23 v 1 No 4 169-70 Plague Outbreak in
Western Yunnan, China.

Plague has been endemic near the border between northern Burma (Shan States) and the Yunnan Province of China for a long time and breaks out almost every year in neighbouring villages. In 1939 a severe outbreak occurred at Nankham as a result of movements of population and the employment of labour for the opening of the Burma Road which ended then at Teng Yoch (Tengchung). Early in 1940 bubonic plague occurred in Yunnan Province at Mungmao near Shweli River and later at Cheshunkai and Nwangtao on the Burma side of the border it appeared at Muse (opposite Mungmao) Selang and Nankham in the Bhamo district.

In January 1945 the National Health Administration of China stated that bubonic plague had broken out around Tengchung (Teng Yoch) situated a few miles west of the Burma Road, and also at Nangtien 25 miles south of Tengchung. A medical expedition to the area was organized and a preliminary report has been received from Dr Y. N. YANG Senior Technical Expert of the National Health Administration.

Plague appeared in September 1943 at Tahungchuan about two days walk from the Burma border in this village of 1,000 families, 140 deaths occurred from February to May 1944. In June 1944 plague occurred in a group of about 50 villages called Lo Pu Shih Chuan about two days walk north of Tahungchuan there were 136 cases and 105 deaths chiefly in July and August. Some cases also occurred at Chi Mu Tsai north of Lo Pu Shih Chuan.

The outbreak at Tengchung (Teng Yoch) was reported early in October 1944 and at Nantien early in November up to January 9 1945 there were 102 cases and 23 deaths. The incidence was highest among children and young adults but the case mortality was 11.4 per cent in the group under 30 years of



Map of the Yunnan Province of China in relation to bordering countries and the Burma Road.

[Reproduced from the *Bulletin of the Health Organisation League of Nations*]

age and 50 per cent in those over 40 years. Sixty-nine of the 102 patients had had one to four inoculations of plague vaccine—the mortality rates were 14.5 per cent in inoculated and 41.4 per cent in uninoculated persons.

Sulphathiazole, sulphadiazine and serum were used in treatment. Sulphadiazine gave the best results—one death in 27 cases—but the author reserves a final opinion on methods of treatment.

Many dead rats were found in the villages where human plague occurred.

J. F. Corson

SHIH F. I. & POLLITZER R. Some Observations on the relation between Rodent and Human Plague. *Chinese Med J* (Chengtu Edition) 1944 Jan. v. 62A No 2 45-51 4 graphs

The rodents referred to in this article are not sylvatic but domestic—the chief cause of human plague. An account is given more or less in diary form of the correlation between degree of incidence of plague in the rat population and its seriousness for the human population. It is illustrated by graphs and tables and the argument used is that a forecast can be made—at least under the conditions obtaining in Central China—of the imminence of a critical situation by close study of the frequency with which plague is occurring among rodents.

A conclusion is worded thus — "the situation remains reassuring as long as the incidence of infected rodents remains well below 20 per cent. The condition must be considered as critical when this level is approached or reached human plague becomes imminent if a level of 25 per cent. is reached or exceeded.

W F Harvey

POLLITZER, R & LI C C. Some Observations on the Decline of Pneumonic Plague Epidemics. *Chinese Med J* (Chengtu Edition) 1944 Jan v 62A No 2, 52-5

China must have vivid recollections still if only in the literature of the subject of pneumonic plague. Reference is made by the authors to the usual statements that decline of pneumonic plague in a community is due to the measures adopted or to seasonal influence. Their own analysis of their cases, recorded in detail leads to the conclusion that the occurrence of primary pneumonia in plague depends on contact with a patient already suffering from pneumonia and exhibiting a bloody sputum and cough. When patients begin to show absence of these features the plague becomes non-pneumonic and the epidemic is declining.

W F Harvey

SHIN F I CHANG S S & YUAN K L. A Report on some Simple Measures for the Control of a Rural Plague Outbreak. *Chinese Med J* (Chengtu Edition) 1944 Jan v 62A No 2 56-60

The measures described have reference to two towns of about 1,600 and 1,700 inhabitants. Many of these were of the usual antiplague description such as quarantine, anti-rat and anti flea measures and rat poisoning. In one of the two towns plague seemed to be restricted to the northernmost part which could be segregated and was segregated by cutting a connecting bridge over a strip of water and by digging a 10-foot ditch to cut off communications. Pickets of soldiers were employed to enforce segregation and watch was kept to prevent inhabitants from taking patients or dead bodies out of the plague area, carrying out bedding and household goods and making journeys which had no relation to business. All cotton shops in the segregated area were closed and their stocks sealed. Export of rice, cotton and other goods apt to harbour fleas was prohibited. Material destined for the army consisting of 2,000 bales of cloth had to be allowed export and was disinfested mechanically by exposure to air and sun. The description is useful in showing how special measures may have to be adopted applicable mainly to local conditions.

W F Harvey

HAYE L T. Experimental Studies on Living Plague Vaccines. *Chinese Med J* Washington, D C 1944 Apr-June v 62 No 2 193-6

Comparisons have been made of the protection afforded in guinea-pigs by dead plague vaccines and by agar slope cultures of attenuated living organisms. Attenuation was effected by growing virulent plague bacilli, obtained from the inguinal gland of a fatal case of plague at 41-42°C. The strain was well attenuated after 16 months of subculture and by the 33rd generation. A testing subcutaneous injection of virulent bacteria obtained from the spleens of rats infected with virulent culture was given three weeks after immunization with various doses of attenuated organisms and immunization was considered to be satisfactory if the guinea-pigs were still alive one month later. A secondary research was made into the power of living plague vaccines to penetrate to the internal organs. Results are summarized as follows — (1) All dead antiplague vaccines used were unsatisfactory. (2) Attenuation of virulent plague bacilli

could be effected by subculture at high temperature. (3) A spontaneously attenuated strain Ming 2 had much better immunizing power than the artificially attenuated organism. (4) The antigenic potency of living plague vaccines is higher the further they can be shown to diffuse from the site of injection to internal organs.

W F Harvey

DEVIGNAT R. L'aération des milieux liquides de culture par barbotage d'air. Le bacille de Yersin en milieu aéré. Observations complémentaires. [Aeration of Fluid Culture Media. *P. pestis* in Aerated Media. Supplementary Observations.] *Rec Trav. Sci. Méd. Congo Belge* 1945 Jan. No 3 112-19 [18 refs.]

This is a version in French of the paper abstracted in this *Bulletin* 1944 v 41 668

CHOLERA.

BURROWS W. The Endotoxin of the Cholera Vibrio. Isolation and Properties. *Proc Soc Exper Biol & Med* 1944 Dec. v 57 No 3 306-8 [10 refs.]

Both the Inaba and Ogawa vibrio types were used and toxic solutions of the cell substance have been prepared in the following ways:—(a) Disintegration by high speed grinding for 4-5 hours with sand to obtain a toxic opalescent supernatant fluid. (b) solution of cells in 6 M urea. (c) digestion with pepsin 3-5 days without inactivation of the toxicity and centrifugation to give a toxic supernatant fluid. (d) extraction in the cold with M/2 trichloroacetic acid which was the first method used. (e) extraction of lyophilized cells with methyl alcohol, ethyl alcohol, chloroform or ethyl ether. The extracted material appeared to be a mixture of lipids, contained inorganic salts, was yellowish in colour and was negative to the Molisch, Millon and biuret tests in alcoholic solution or in aqueous suspension. It could be consistently obtained with a mouse m.l.d. of 30 µg. In general it became clear that the endotoxin of the cholera vibrio is (a) resistant to peptic or tryptic digestion, (b) stable to acid, (c) unstable to alkali (N/10 NaOH at room temperature), (d) readily soluble in methyl and ethyl alcohols, chloroform and ether but not in glycols, (e) readily dialyzable and (f) is closely associated, possibly identical with a phospholipid.

W F Harvey

BURROWS W, MATHER Adaline N, WAGNER, Sylvia M & MCGANN Virginia G. The Endotoxin of the Cholera Vibrio. Immunological Properties. *Proc Soc Exper Biol & Med* 1944 Dec. v 57 No 3 308-11

Some of the work which has previously been done is irrelevant because it relates to a toxic haemolytic vibrio whereas the true cholera vibrio is non haemolytic. Various preparations of cholera endotoxin have been studied by the authors and immunological activity demonstrated by skin reactions in immune rabbits by specific precipitation and by complement fixation with rabbit immune sera. These tests appear to show that endotoxin preparations have haptene-like functions although the antigen-antibody reactions have not proved useful for routine purposes. It has been found possible to immunize mice actively by inoculation of alcohol-saline suspension of alcoholic endotoxin.

On the other hand it has not been possible to demonstrate *in vitro* neutralization of the activity of endotoxin preparations by either antibacterial or anti-endotoxic sera known to be protective when tested against mucin vibrios in the mouse.

W F Harvey

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some days after the drug is stopped. Increases in the blood-iodine levels from 45-6 microgrammes to 437.25 milligrammes have been noted in man and experimental animals. In the present series of 78 cases two of intolerance to diodoquin were observed, and two patients complained of mild pruritus ani the drug throughout the large intestine.

Three tablets of diodoquin (each of 3.2 grains) three times daily for 20 days was the standard dosage. In addition in another series of cases diodoquin was combined with quinoxyol retention enemas for 10 days and a small series which showed either amoebic hepatitis or other evidences of deep infections, received emetine injections as well. A small unselected control series treated with E. B. I. and quinoxyol enemas has been included for comparison. All the patients were sigmoidoscoped before and after treatment and in 13 the treatment was carried out on the basis of sigmoidoscopic appearances alone the stools being negative at the time although in all of them *E. histolytica* had previously been found.

SERIES I. Twenty six cases were treated with diodoquin by the mouth. Seventeen of these were apparently cured. Follow-up examinations of three stools were negative two months after discharge from hospital. Two of the patients had received no previous treatment. In addition in three cases with positive sigmoidoscopic findings, but negative stools the lesions healed at the end of treatment. There were two relapses and four cases were resistant. In one of these amoebic abscess of the liver developed three months later. Another patient had an acute relapse and his case had been particularly resistant to previous forms of treatment. Another presented petechial haemorrhages in the rectum at the end of one course and yet another relapsed four months after treatment.

SERIES II. Cases treated with diodoquin for 20 days plus quinoxyol retention enemas for the last 10 days of the course. This combined treatment was initiated on the grounds that lesions in the rectum might not be exposed long enough to diodoquin in the lumen of the bowel. Logically it would have been better to have used diodoquin retention enemas. This was done successfully in one case but it could not be pursued as supplies of the drug were restricted. Thirty-nine cases were treated in this series with results as follows:—22 cured (stools positive for *E. histolytica* before treatment) 8 cured (stools negative but sigmoidoscopically typical) 2 were resistant and 7 relapsed.

SERIES III. Emetine hydrochloride 6-10 gr by mouth plus diodoquin currently by mouth for 20 days for the last 10 days the patient also received quinoxyol retention enemas without a preliminary bowel washout. This treatment was carried out in those cases showing symptoms of hepatitis gross deep ulceration or marked leucocytosis. The results were:—9 were apparently cured having had stools positive for *E. histolytica* before treatment 2 were apparently cured having had stools negative before treatment 1 relapsed. I was resistant. In one patient petechiae were present in the rectum after one course. He was then given E. B. I. and quinoxyol and a further sigmoidoscopy showed a normal mucosa.

SERIES IV. Standard combined course. E. B. I. 3 gr in cachets by mouth together with a cleansing bowel washout of 2½ per cent soda bicarb. solution followed an hour later by 250 cc of 2½ per cent quinoxyol which was retained for 6-8 hours. This treatment was carried out for ten days and was then followed by carbazone 4 gr b.i.d. for 10 days. There were 24 cases in this series. 16 were cured relapsing. Three primary cases were cured. Two of the relapsed cases were subsequently cured with diodoquin. In 5 examination of the stools was negative but sigmoidoscopy showed either ulcers or pits. Two cases were resistant to all forms of treatment.

Two instances of intolerance to diodoquin were encountered. One patient on the 14th day of treatment with this drug, had abdominal pain diarrhoea blood and mucus in stools full of *E. histolytica*. He responded well to emetine and tolerated a second course of diodoquin and quinoxyl retention enemata with no further ill effects. The second a severe case with Dyak-hair sloughs in the rectum and *E. histolytica* in the stools complained on the 14th day of abdominal pain diarrhoea and headache. The symptoms were rapidly relieved by emetine. A further course of diodoquin E.B.I. and quinoxyl was well tolerated, and sigmoidoscopy showed complete healing of the ulcers.

The histories of two specially severe cases are given. One was treated with diodoquin alone the other received a course of emetine plus diodoquin. The first exemplified how by erratic and inefficient initial therapy a case is rendered emetine resistant and how quickly it may respond to diodoquin. The second had had unrecognized amoebiasis of over 24 years standing before the correct diagnosis was made. In October 1944 the stools were found to contain active *E. histolytica* which emanated from a large rectal amoeboma 4 in from the anus suggestive of an adenocarcinoma. On a course of six daily 1 gr. injections of emetine together with diodoquin for 20 days and treatment with quinoxyl retention enemata and stovarsol this amoeboma healed up. The patient subsequently received a 10-day course of E.B.I. and quinoxyl. Three months later sigmoidoscopy revealed a normal mucosa.

Diodoquin then appears to be the best of the oxyquinoline group of drugs in the treatment of amoebiasis and is a valuable addition to the list of remedies. It is non toxic in therapeutic doses. The practice of treating amoebiasis with emetine alone cannot be too strongly condemned as only a small percentage of cases are cured whilst the vast majority are rendered more resistant to further treatment with emetine and less amenable to other available drugs.

P. Manson Bahr

CHENG Wen Szu, LIU You Ping & TAN Shih-Chien. Toxicological Investigation on Ya Tan Tzu. *Chinese Med J* (Chengtu Edition) 1944 July v 62A No 4 133-9 [10 refs.]

Ya Tan Tzu, the seed of *Brucella javanica* has been given in China for the treatment of dysentery during the past 180 years perhaps longer but its composition and mode of action have never been closely studied. At all events no very conclusive results have been reached. Some have reported the active principle to be a glucoside others a saponin others again an alkaloid.

The authors have obtained and tested the expressed oil, a volatile oil distilled by steam from this ether, chloroform and alcohol-extracts of the oil free portion using cats, dogs and rabbits as their experimental animals and administering the various preparations by stomach tube and by injection hypodermic and intravenous.

It is the oil free part which is toxic to animals whichever route of administration is used when given in amounts of 0.19 gm. per kilo body weight. It causes nausea, salivation, vomiting, passage of blood in the stools and vomit, convulsions and death. The alcoholic extract causes no more than a fall of arterial pressure which soon passes off. The volatile oil is a slight gastro-intestinal irritant but the only part of the seed is not poisonous nor did the ether extract cause any symptoms. At autopsy there are signs of haemorrhage in the stomach and intestine (both small and large) and the mucosa is swollen and congested. The liver is enlarged and congested with leucocytic infiltration, fatty degeneration and vacuolization of the cytoplasm especially in the mid-zonal area but also in the periportal and central. The kidneys are congested.

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the convoluted tubules almost obliterated by the swelling of the lining cells the spleen is congested and may show haemorrhages the cerebral vessels are engorged [as would be expected in death after convulsions] H Harold Scott

FAIR G M CHANG S L TAYLOR, Margery P & WINEMAN Margaret A.
Destruction of Waterborne Cysts of *Entamoeba histolytica* by Synbiotic Detergents. *Amer J Pub Health* 1945 Mar v 35 No 3 228-32.

The authors have tested the cysticidal activity of a number of cationic, neutral and anionic synthetic detergents by exposing cysts of *Entamoeba histolytica* suspended in a quart of water to their action. After exposures of from 15 minutes to 2 hours the cysts were washed and their viability tested by inoculating them to culture media. It was found that the cationic detergents were superior to the others. Thus the most successful were effective in one-third to one-fifth the concentration required for the neutral heavy resorcinol, while the anionic detergents were not cysticidal in the concentrations tested. The successful detergents required a concentration ten times as great as that necessary for chlorine which has been shown to be approximately 3 p.p.m. 2 p.p.m. and 1 p.p.m. for exposures of 15, 30 and 120 minutes respectively [this Bulletin 1942 v 39 313 these are doses not residual values]. One advantage of the detergents over chlorine is that the activity is not affected by the presence of organic matter in the water while changes in hydrogen-ion concentration had little if any effect. A definite disadvantage is that water containing a detergent even in the minimal effective concentration tends to froth when shaken. Furthermore there is a complete lack of information regarding any physiological effect the synthetic detergents may have on human beings.

C M Henson

RELAPSING FEVER AND OTHER SPIROCHAETOSSES

CHEN Y P ZIA S H & ANDERSON H H Immunity Reactions in Experimental Relapsing Fever. *Amer J Trop Med* 1945 Mar v 25 No. 2, 115-16

The authors infected two *rhesus* monkeys with a Californian tick-borne strain of *Spirochaeta recurrentis* by the intraperitoneal inoculation of blood from infected Chinese hamsters in doses of 0.02 cc per kilo.

Both monkeys showed spirochaetes in the peripheral blood 60 and 73 hours after inoculation and the blood remained positive for 24 to 36 hours. Seven days after the blood had become negative a second inoculation was given with double the initial dose but neither spirochaetes nor febrile symptoms were noted and a third inoculation also produced no obvious effects. Twenty-eight and 33 days after the disappearance of spirochaetes from the peripheral blood biopsies were performed and in both animals spirochaetes were found in the grey matter and blood vessels of the brain.

Subsequently each monkey was inoculated with 2.0 cc of blood from a patient infected with a Chinese louse-borne strain of relapsing fever but no spirochaetes were observed during a 31-day period of examination. Brain tissue removed from the monkeys at a second biopsy 50 and 54 days respectively after the first showed no spirochaetes in the frontal lobe area.

Four Chinese grey hamsters *Cricetus griseus* were splenectomized and inoculated with a Chinese strain of relapsing fever. Three of the four

spirochaetes in the peripheral blood 4 to 6 days later. After 23 days these hamsters were inoculated with the Californian strain and all showed spirochaetes in the blood but for a short period only in contrast to the 3 to 4 attacks seen in control animals. The brains of these hamsters contained spirochaetes.

Hamsters inoculated with brain tissue containing spirochaetes did not show any signs of infection and when inoculated with infected blood developed normal infections. There was no appreciable difference in the infectivity of hamster blood containing spirochaetes which was mixed with brain tissue and kept for 22 hours in the ice box and similar blood to which no brain tissue had been added.

These results support the view that residual infection plays an important rôle in the immunity which develops after an attack of relapsing fever. They also indicate that cross-immunity exists between infections with the Californian and Chinese strains of *Spirochaeta recurrentis*.
E Hindle

MAY W K C. Relapsing Fever with Meningitic Manifestation. A Case Report. *Chinese Med J* (Chengtu Edition) 1944 July v 62A No 4 142-3

A fatal case of relapsing fever in Yunnan is reported. The meningitic manifestations were marked and abundant spirochaetes were recovered from the cerebrospinal fluid following repeated negative blood smears.

SCHUHARDT V T & O'BRYAN B E. Effect of Intracranial Penicillin Therapy on Brain Involvement in Experimental Relapsing Fever. *J Bacteriology* 1945 Mar v 49 No 3 312-13

In a previous paper [this *Bulletin* 1945 v 42 387] the authors reported that in rats infected with *Spirochaeta recurrentis* (novys) intraperitoneal injections of penicillin which would cure the blood infection and prevent the cerebral infection failed to cure the cerebral infection. In the experiments here reported combined intracranial and intraperitoneal injections of penicillin were used.

Seventeen rats infected 12 to 40 days before were divided into six groups containing 3 3 3 3 2 and 3 rats respectively. Each of the rats of Groups I, II and III received 1 000 units intracranially and 400 units every 3 hours for 48 hours intraperitoneally. Group I rats had a single intracranial injection. Group II had two intracranial injections of 500 units and Group III had three intracranial injections of 333 units. Group IV rats received intracranial injections of buffer solution (penicillin diluent) the same dose of phenobarbital (for anaesthesia) as the test rats and the same total dose (7,800 units) of penicillin as the test rats in 17 intraperitoneal injections. The 2 rats of Group V had no phenobarbital and no intracranial injections, but they had the same amount of penicillin in 17 intraperitoneal injections. Group VI rats were not treated.

Two days after the end of penicillin treatment the brains of the rats were emulsified and passed to fresh rats. Those of the test rats caused no infection while the brains of the control rats did. It would appear therefore that intracranial injection of penicillin can cure the brain infection in experimental relapsing fever in white rats.
J F Corson.

KAPLAN Dora. Studies on the Cultivation of *Borrelia Gallinarum*. [Summary of Thesis for the Degree of Ph.D.] 3 pp. [Submitted to the Senate of the Hebrew University, Jerusalem July 1944.]

The following medium was found satisfactory for the culture *in vitro* of *Borrelia* [*Spirochaeta*] *gallinarum* —

A Basic salt solution 1 000 cc. proteose Difco peptone 4 gm. dextrose 1 gm. thuyglycolic acid 0.1 gm.

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B Before inoculation add to 10 cc. of A 1 cc. of fresh rabbit serum and 0.6 cc. of chicken red cells resuspended in an equal volume of basic salt solution. Instead of adding the chicken red cells they may be haemolysed with 3 volumes of water and the supernatant fluid, after centrifugation used instead of the red cells.

The basic salt solution has the following composition: NaCl 5, Na_2HPO_4 2.5, KH_2PO_4 0.25, MgCl_2 0.3, FeSO_4 0.0003, MnSO_4 0.0005 and H_2O 1000.

The spirochaetes were cultured on this medium for more than 30 months and retained their virulence for at least 13 months at 16 months they were found to be avirulent but they still produced specific immunity in fowls, lasting for at least 7 months.

Various modifications produced by adding substances to the medium, were tested and were found to promote growth of the spirochaetes in varying degrees.
J. F. Corson

14WS

STATAUX R. Deux cas de pian avec lésions bilatérales d'hyperostose péri-orbitaire. (Two Cases of Yaws with Bilateral Periorbital Hyperostosis.) *Rec. Trav. Sci. Méd. Congo Belge* 1945 Jan. No 3 177-81 2 figs.

Two cases of yaws with very early development of osseous lesions including the involvement of the orbital margins are reported.

The first patient was an African girl, aged 15 years. She had numerous small ulcers more like ecthyma than yaws on her right breast, she had numerous small various parts of the body. The bones affected were the superior maxillary and malar bones the bones of the forearm, the right scapula, right calcaneus and right first metatarsal. The first sign of the disease appeared about 3 weeks before as a small tumour on the right breast which ulcerated after 3 or 4 days about a week later her breast was covered with small ulcers and the bony swelling appeared about the same time. The facial swellings involved the orbital margins formed by the superior maxillary and malar bones of both sides, and on the left side the orbital part of the frontal bone also. Her face had a somewhat Mongolian appearance.

The second patient seen in the same month, was an African woman, aged 45 she had characteristic yaws lesions on the skin of her left calf and bony swellings involving the orbital margins formed by the superior maxillary and malar bones the left clavicle left scapula and the distal end of the right tibia also showed swellings.

Both patients were cured within 2 months with bismuth. The author remarks on the rareness of such orbital lesions although his hospital dealt with over 2,000 new cases of yaws a year he had never seen a similar case in nine years, nor had a case of gonorrhoea been met with. Another point of interest was the very early appearance of the bone lesions in the first patient.
J. F. Corson

LEPROSY

AUSTIN C. J. Central Leper Hospital Makogai, FIJI. 19 pp. 21 figs. 1944
Nov. 28. Issued by the Information Office Fiji.

This is a well-illustrated general account of the Makogai Leper Hospital, by its superintendent, Dr. Austin, which has been published by the Fiji Government. The hospital is situated on a beautiful island 3 miles from Suva.

separate villages for patients of different races from Fiji the Solomon Cook and Gilbert Islands. A general hospital is well equipped and includes an X ray apparatus. Missionary sisters superintend the nursing and train numerous native nurses. The able-bodied patients are employed on agriculture fishing building etc. which reduces the cost of upkeep and enables the sufferers to earn money. Religious services sports concerts and other amenities are provided and a New Zealand Leper Trust furnishes a comforts and Christmas Day fund. An increase in the Fijian patients from 352 in 1919 to 444 in 1943 is due to earlier admissions for the early neural cases have greatly increased but the lepromatous admissions have fallen from 32 to 0. In 1928 1 000 trees were raised from seed sent by B.E.L.R.A. which provide half the hydnocarpus oil used in treatment. On an average 40 patients have been discharged yearly with only 10 per cent. of relapses during the last 10 years. Compulsory isolation is in force and under the very favourable conditions provided for the inmates it is considered to be a success. The Fiji Government have done well in publishing this report which should stimulate leprosy institutions in other British colonies to emulate the Fiji example of humane and efficient control of the disease.

L. Rogers

BRITISH GUIANA. Annual Report. Leprosy Hospital, Mahaica, 1944 [WHARTON L. H. Med. Supt.] MS 16 typed pp

Dr Wharton was confirmed as medical superintendent from the beginning of 1944 in succession to the late Dr Rose. This report shows that the subordinate staff consists of 52 males and 21 females. Sanitary measures have reduced the incidence of flies and mosquitoes. Improved bread has been supplied and the co-operative spirit and mental outlook of the patients have improved with the provision of employment for 200 of the patients and recreations cinema etc. with the help of a special committee. During the second half of the year 6,830 children were examined and 22 early cases of leprosy were detected. It is hoped soon to be able to examine all contacts of patients in their homes. Treatment has followed the usual lines for 300 in patients 591 others attending clinics out of a total of 995 patients, 356 of whom were in hospital. The medical board admitted 35 new cases and discharged 23 on parole. The deaths amounted to 34 (9.5 per cent.) 10 of these were from septic complications 5 from chronic nephritis and 9 from senile or general debility. Most of the patients are Africans East Indians mixed and Portuguese in that order of frequency the Portuguese numbered 24. The report closes with the statement that there has been definite progress during 1944 in the control of leprosy both from the treatment and public health aspects.

L. Rogers

HOPKINS R. & FAGET G. H. Recent Trends of Leprosy in the United States. Report of Seven Hundred Cases at the National Leprosarium. *J Amer Med Ass* 1944 Dec 9 v 126 No 15 937-43 1 chart

This is an instructive analysis of the leprosy cases in the National Leprosarium from 1928 to 1944 during which period there were 723 admissions. The present data are compared with those of 1921 to 1928. A table of State admissions during the two periods shows a notable increase of admissions from Texas in the second period many of these were found to have been infected in Mexico. They now exceed those from Louisiana itself. California and Florida have the next largest number of endemic cases and Florida, Illinois and New York had a number of new admissions most of which were imported cases. The number in these States has remained fairly constant. The imported cases nearly all (221 out of a total of 303) came from Mexico the Philippines British West Indies and China. A great decline in the cases from Massachusetts and

Type	L 3	L 2	L 1	N 1
Cases Positive	40 57.5 per cent.	45 36 per cent.	55 22 per cent.	30 10 per cent.

He therefore concludes that the Kahn reactions are reliable in leprosy as well as in syphilis.

KIRKALDY WILLIS W. H. Sympathectomy in Leprosy. *East African Med J* 1945 Mar., v 22, No 3 88-90
L. Rogers

An African man aged 40 had had a pricking sensation and burning pain all over his body for 18 months pain in the wrists and hands for 12 months, numbness of the fingers of the right hand for less than 12 months and a spreading ulcer on the outer side of his right foot, involving the little toe for 3 months. He was gradually losing weight.

On admission he was wasted and anaemic (Hb. 70 per cent.) both hands and the whole left forearm were insensate the small muscles of both hands were wasted and paralyzed, both thighs and legs showed loss of sensation, both knees and ankle jerks were increased, and there were light-coloured patches on the front of the chest and abdomen. There was a deep necrotic ulcer 2 x 4 inches in size on the dorsum of the right foot involving the little toe the two distal phalanges of which were exposed and necrotic.

Operation.—Under spinal anaesthesia, the right superficial femoral artery was freed from its sheath for 2 inches in the lower part of the femoral triangle after dividing 2 or 3 small branches the adventitia was injected with normal saline alcohol, the excess being washed off with saline. The artery contracted to about one-third of its normal diameter and its pulsation was much diminished. The sheath was sutured and the wound closed. The ulcer was then excised, dressed with iodoform in paraffin.

Four days later the ulcer showed red granulations but an abscess appeared on the outer border of the left foot and was incised. Ten days later the ulcer was clean and red, the incision in the thigh had healed, and the incision on the left foot had almost healed. After another 8 weeks the ulcer had quite healed. The author has no doubt that the operation on the femoral artery produced more rapid healing than would otherwise have occurred he observed that the right foot remained warmer than the left for about a month after the operation.

SAGHER, F. Effect of Grenz Rays on Leprous Infiltrations. Report of an attempt to influence Leprous Infiltrations by Roentgen Rays of Long Wavelength. *Arch Dermat & Syph* 1944 Nov 50 No 5 311-14
J. F. Corson

The author points out that early trials of roentgen and radium rays in the treatment of leprosy nodules were rather unfavourable and might cause severe damage to the surrounding skin and underlying organs. He has therefore tried the far less dangerous Grenz rays in doses of 800 to 8,000 rk. in a single exposure or in several fractional exposures in a total of 18 selected cutaneous areas, all of which showed numerous lepra bacilli before treatment. The recorded details of repeated exposures in two well-developed mixed cases show that only doses of 2,000 r and upwards were effective, larger doses

used in proportion to the amount of infiltration of the selected erythematous patches. After four months to one year the skin lesions became clinically free from symptoms but the general course of the disease was not modified, although when new cutaneous lesions appeared almost all the irradiated areas were spared and the advance of the process halted abruptly at the border of the treated areas. Moreover histological examinations showed that both the cellular infiltration and the number of Hansen's bacilli were greatly decreased in the treated areas as compared with the immediately surrounding unexposed skin lesions. The author therefore advises the use of Grenz rays in the case of disfiguring lesions especially those on the face

L. Rogers

ZANETTI, V. Lèpre et prophylaxie au Congo Belge. [Leprosy and its Control in the Belgian Congo.] *Rec. Travaux Sci Méd Congo Belge* 1945 Jan No 3 96-108.

This paper gives a long general account of a system of agricultural village isolation of lepers (V.A.L.L. for short) in the Belgian Congo. Total compulsory segregation is not advised for the estimated 60 000 cases but numerous agricultural villages are being organized, each to provide for 300-400 cases visited once or twice a week by a medical officer and with work for the able-bodied to reduce the cost and to provide food. A plantation of *Hydnocarpus* trees in each will furnish the oil for treatment. Indirect and mild pressure is used to obtain admission of infective cases. Only uninfected patients are allowed to visit their homes but visitors can come to the boundaries to see their relatives. The isolation is more or less voluntary in most cases and the cost is moderate. All possible social amenities are provided. A home is provided for the healthy children of patients. The original diagnosis and examinations before discharge when the disease is arrested are always made by doctors with bacteriological tests. In treatment a mixture of *Hydnocarpus* oil and sodium gynocardate is much used.

L. Rogers

DELPÉRDANGE, G. Sur la présence probable du bacille de Stephansky à Coquilhatville. [The Probable Presence of Rat Leprosy in Coquilhatville.] *Rec Travaux Sci Méd Congo Belge* 1945 Jan. No 3 109-11

This note reports that acid fast bacilli were found in 52 of 470 rats examined (9 per cent.) One showed lesions of the skin internal organs and glands containing very numerous acid fast bacilli and microscopical changes characteristic of rat leprosy. An inoculated white rat developed similar lesions after several months, but attempts at cultivating the bacilli have been negative. Guinea pigs were negative to inoculation and so was a monkey at the time of reporting. The author concludes that it is probable that rat leprosy occurs in the Belgian Congo but further work is required to establish this.

L. Rogers

HELMINTHIASIS

KUO Shao-chou & KIANG Lin-mei. The Animal Parasites of Dogs in Chengtu. *Chinese Med J* (Chengtu Edition) 1943 Oct v 62A No 1 15-18.

E. C. FAUST in 1929 reported his results from an investigation of the animal parasites of dogs and cats in China. H. T. CHEN studied in 1934 the helminths of dogs in Canton [this *Bulletin* 1935 v 32 620]. T. H. CHIN and K. C. LI the

parasites of dogs and cats in Kweiyang [ibid., 1943 v 40 847], and the same authors with K. CHANG and W. K. TONG ankylostomiasis in Szechwan [ibid. p 831].

The authors of the present paper examined carefully 40 stray dogs caught in the streets of Chengtu. They found ectoparasites of *Ctenocephalus felis* and *Pulex irritans*. *Trichostrongylus axei* species of *Amblyomma* and *Haemaphysalis*

The helminthic parasites were of much interest. All 40 showed some helminthic infestation. Thirty-six were harbouring *Ancylostoma caninum* on an average less than 20 per dog, but one had 73. *A. braziliense* which has been reported in Chengtu, was not found among these. *Toxocara canis* was found in 12, but in one only (which contained 15) was the number over 10. *Dirofilaria immitis* was present in the hearts of four in large numbers and in one there were three specimens of *Spiracera sanguinolenta* in an oesophageal tumour. Twenty four of the 40 were infested with *Dipylidium caninum* one had as many as 143. Eight harboured *Diphyllobothrium mansoni* but no case of human sparganosis has been recorded in Chengtu. *Taenia* [species not stated] two five specimens of *Echinococcus granulosus* were found in one dog, the only one of the 40 found thus infested. *Metagonimus valagrensi* was found in seven, but only one was heavily infested (172 specimens). *Echinochasmus perfoliatus* in two and *Paragonimus* sp. in one (four flukes being present). *Clonorchis sinensis* common in cats was not seen in any of the 40 dogs. It is noted that corn-sweet-potato growers in Northern Szechwan suffer severely from ground-itch and that dogs faeces are used frequently as fertilizer. It would be interesting to examine the local inhabitants especially the agricultural workers for infestation by *Ancylostoma caninum*.

ANDREASSEN, A. T. & SUMI, H. L. A Case of Schistosomiasis Infection contracted in India. *Indian Med Gaz.* 1945 Feb v 80 No 2 93-4

H Harold Scott

This appears to be the first recorded case of infestation with *Schistosoma haematolum* having been acquired in India.

A Sepoy aged 19 with four months military service was admitted to hospital at Rawalpindi Punjab suffering from haematuria which was thought to have been due to an injury received while playing hockey a fortnight before. Ova of *S. haematolum* were found in his urine and on cystoscopic examination the bladder had the typical appearance of schistosomiasis. No evidence of intestinal schistosomiasis was found.

The patient was said not to have been outside his native district of Ropar Ambala Punjab except for a short visit to Poona and his military posting to Rawalpindi. As the disease was well established it is thought probable that he contracted it in his native village of Talapur and that intermediate snail hosts must exist there (possibly at Poona) it had not yet been possible to investigate this.

The authors mention the obvious importance of this case in view of the movements of troops between India and countries where the disease exists.

J. F. Corson

BARNETT, L. Hydatid Incidences in New Zealand for the Year 1943. *New Zealand Med J.* 1945 Apr 44 No 240 99-100

WAR OFFICE ARMY MED DEPT BULL. No 47 1945 Mar 2-3 Ancylostomiasis complicating other Disease—A Reminder

Doctors both service and civilian are not perhaps aware how often white troops may have hookworm ova in the stools after service in an area where

infection is common among the native population. Symptoms are uncommon and infection may not become apparent unless the men are investigated in hospital for some other disease. Relapsing malaria especially in personnel returning from the Far East may be complicated by infection with one of the varieties of *ancylostoma*. An eosinophilia of more than 5 per cent is suggestive of infection and a haemoglobin of less than 80 per cent may be due to a long standing and heavy infection. In either case examination of the stools should be made.

In an Australian General Hospital an investigation was made to find out the frequency of hookworm infection among white troops.¹ Stools and blood of 2 000 patients were examined. About 1 600 of these had served in New Guinea for periods varying from a few weeks to 18 months. Eight hundred men were excreting hookworm ova. Laboratory culture of the ova from the faeces of a small sample of the group showed that half were infected with both *Ancylostoma duodenale* and *Necator americanus*. In most the infection appeared to be light and it was estimated that they had less than 20 female worms in their intestines. Different brigades showed varying infection rates. In one unit it was 97 per cent.

A history of ground itch or creeping eruption² was not obtained from the patients. This is surprising as the commonest mode of entry of the hookworm is through the hair follicles of the legs. This may follow marching through infected swamps. The ingestion of infected drinking water or uncooked vegetables is a less common route of infection. Many of the men gave a history of vague dyspepsia during their service in New Guinea. In addition to ova occult blood was often found in the stools. Eosinophilia was variable diminishing with successful treatment.

Different methods of treatment were tried. It was confirmed that two drugs in combination gave better results than either used alone. In the British Army³ this has also been the experience and it is advised that tetrachlorethylene should be used in combination with oil of chenopodium. The drugs are mixed together 4 c.c. of tetrachlorethylene and 1 c.c. of oil of chenopodium. This draught is given in the early morning on an empty stomach, no food being allowed until the bowels have been satisfactorily moved. If necessary this may be assisted with a dose of epsom salts a few hours later.

The effects of treatment may be judged by the number of ova found in the stools, the degree of eosinophilia, and the cessation of symptoms if these have been present. In about a quarter of the cases two or more courses are required to eliminate all worms, but it should seldom be necessary to hospitalise men for more than a few days on account of uncomplicated ancylostomiasis. The finding of an occasional ovum is no justification for retention in hospital.

It is always wise to consider ancylostomiasis as a cause of uncomplicated anaemia. A heavy infection may cause a considerable degree of anaemia resistant to treatment until the infection has been eliminated.

TANG W. K. & CHANG K. Symptoms of Hookworm Disease. Reprinted from *Chinese Med J* (Chengtu Edition) 1943 Oct v 61A 105-6

This is a short note of the symptoms found in 44 patients severely infected by hookworms (*A. duodenale* and *N. americanus*) in Szechwan. For their information the authors relied largely on the patients' own statements. The most common complaints were—ground itch, cough, intestinal discomfort, diarrhoea alternating with constipation, geophagy, cardiac palpitation, tinnitus and

¹ Unpublished report 1945 RFA (45) 3 Australian Army Staff London.

² *This Bulletin* 1944 Oct. No. 40 article 312.

³ *Memoranda on Medical Diseases in Tropical and Sub-Tropical Areas* War Office 1942, page 10

muscular weakness. The cough was sometimes associated with asthmatic symptoms started 2-10 days after the appearance of ground itch and lasted for 2-3 months. [In a patient with such a history a sputum examination for tubercle bacilli would be advisable.] There was no definite relation between intensity of infection and haemoglobin percentage, but the haemoglobin values of these patients were very low. [Much modern work indicates that symptoms of hookworm disease are unlikely to appear unless there is some degree of malnutrition. If this is so it seems possible that some of the symptoms noted above may have a nutritional, as well as a hookworm basis.] Charles Wilcocks

CHANG K. & CH'EN H. T. An Evaluation of Pickled Vegetables in the Dis-semination of *Ascaris lumbricoides*. Reprinted from *Chinese Med J* 1943 Jan. v 61A, 63-9 2 figs

Infection with *Ascaris lumbricoides* is very common in the Province of Szechwan the incidence varies from 88 to 93 per cent and it is estimated that the average worm burden is about 20 though estimates of over 100 are not uncommon. The authors decided to investigate the possibility that vegetables grown in soil fertilized with human faeces and pickled in brine to which are added wine and sugar might contribute to the spread of infection. The process of pickling which is essentially one of bacterial fermentation is described and it is stated that vegetables pickled in this way form a very large item in the daily diet of the people.

Three methods of examination were used. In the first, brine from the jars containing the pickled vegetables was centrifuged, and the sediment was either examined macroscopically or was subjected to floatation techniques to pick out the eggs. In the second, washings of the pickled vegetables were examined. In the third tests were made of the viability of eggs collected from the faeces of children and kept in brine by observing the embryonation of eggs which were undeveloped at the beginning of the experiment or the vacuolization of embryonated eggs and the activity of the larvae.

The first method revealed 7.14 per cent of positive results in 378 specimens from houses or condiment shops most of the *Ascaris* ova were apparently viable. The floatation techniques were not useful. The second method was a failure. The third method showed that a large proportion of eggs kept in brine at room temperature for 30 days remained viable whether originally undeveloped or embryonated.

Details of the findings are given and the conclusion is reached that pickled vegetables are able to play a part in the spread of *Ascaris* infection though in rural communities there are other more important sources which are responsible for more widespread and heavy infections in West China. The authors also quote from their own unpublished work in which they found that 7.5 per cent of the [presumably fresh] vegetables on Chengtu markets were contaminated with *Ascaris* eggs. Charles Wilcocks

HANG K. TONG W. K. CHEN H. T. & LI C. H. Quantitative Studies on *Ascaris lumbricoides* in Szechwan. Reprinted from *Chinese Med J* 1943 July v 61A 166-9

In this short note the authors record the findings relating to infection with *Ascaris lumbricoides* made during a hookworm investigation in Szechwan. Examination was made by the smear the Willis and the Stoll technique and the result indicated infestation in probably 100 per cent of the inhabitants of certain regions. Children were usually heavily infested, but some adults also had numerous worms. The average *Ascaris* burden for children was 27 for

all ages 17 but burdens of 150 or more were found [These seem to be calculated on the number of eggs passed] Details are given of the findings in various areas
Charles Wilcocks

UNGAR H Complications due to *Ascariasis*, as observed at Autopsy *Harefuah* Jerusalem. 1945 June 1 v 28 No 11 [In Hebrew 237-40 5 figs English summary 240-41]

Post mortem findings in eight cases of ascariasis are reported In six the fatal outcome was directly influenced by the presence of worms The cases illustrate different ways in which ascariasis may be the cause of serious complications. There were three cases of intestinal obstruction with subsequent gangrene of the intestinal wall one case of invasion of worms into the common bile duct and one into the pancreatic duct and three cases of toxic damage to the intestinal wall probably caused by substances produced by the disintegration of dead worms.

All cases but one support the opinion expressed by some authors that serious complications depend not so much on the presence of excessive numbers of worms in the intestines but rather on the coincidence of other pathologic factors which may be summarized as follows

(1) Obstruction may occur as a result of spasmodic contractions of the intestinal wall around groups of worms because of increased peristalsis during febrile diseases acute enteritis amebic dysentery (case 1) reversible torsion due to congenital malformation (case 2) transient interference with the secretion of bile caused by calculi or worms (case 3)

(2) Invasion of the bile or pancreatic ducts is more likely to take place when the sphincter of the papilla of Vater has become inefficient during chronic inflammation (case 4) or in cases of anomalous fusion of the pancreatic and common bile ducts at some distance from the papilla (case 5) Achylia gastrica is considered as a subsidiary factor which enables worms to migrate from their usual site in the jejunum in the direction of the esophagus. It should be mentioned that the diagnosis of worms in the papilla may be confused with the diagnosis of passing gall stones. If worms do not return to the intestinal lumen as may be assumed in case 2, a later sequel of the invasion of worms into the biliary ducts is suppurative cholangitis with the formation of multiple abscesses in the liver (case 4)

(3) Lesions of the lungs in ascariasis are of two kinds. Severe hemorrhages into the lungs have been observed in the course of the developmental cycle of ascariasis during its passage through the pulmonary capillaries (case 2) In an indirect way damage may be done to the lungs when the presence of ascariasis in the stomach induces vomiting and the vomitus is aspirated into the respiratory organs (case 8) The importance of this finding for the development of post-operative pneumonia has been stressed by some surgeons.

(4) Severe lesions of the intestinal wall have been noted in two cases where macerated worms were found in the lumen

Case 7 was that of a young diabetic who was admitted in coma. In spite of adequate anti-diabetic treatment the patient died within 24 hours after admission. Death was caused by peritonitis which started from a necrotic segment of the ileum. The same segment contained groups of dead worms.

Case 8 deserves special attention even in a short review of the original article. A woman aged 28 died 11 days after a gastric resection had been performed for duodenal ulcer For about 8 days following the operation the recovery was uneventful. Then, the patient vomited several worms and afterwards developed signs of bronchopneumonia Towards the end there was evidence of severe hemorrhage into the intestinal tract.

"Necropsy revealed the stomach and duodenal stump filled with dead worms in a state of advanced decomposition. In the duodenum they were enclosed in soft blood clots which covered two round perforations with thin punched-out margins. There was a small amount of blood in the subhepatic area of the peritoneal cavity but no evidence of acute peritonitis. From macroscopic and microscopic examination, the conclusion seemed justified that acute perforation was a sequel to necrosis of the duodenal wall due to the action of toxic substances liberated from the body of dead ascars."

VINSITZKY I. M. A Comparative Study of the Defensive Reaction of the Organism of various Animal Species to parenterally introduced Living Nematodes. C. R. (Doklady) Acad. Sci. URSS Moscow 1944 v 45 No 4 173-8. [In English.]

Using guinea pigs, rabbits, cats, dogs and hens the author surgically introduced into the peritoneal cavity either living or dead *Ascaris suum* (*Ascaris lumbricoides*) and *Toxocara canis* and studied the histological reactions of these animals. [He does not state whether both these nematodes were introduced into all these animals. He does not discuss the fact that the animals used are all unusual hosts for *A. lumbricoides* and that only the dog and cat are normal hosts for *T. canis*. It is well known that the reactions of unusual hosts are more vigorous than those of normal hosts. The author does not mention the work of CHANDLER (this Bulletin 1937 v 34 39) who surgically implanted dead *Aspistrostrongylus muris* of the rat into the body cavity of laboratory rats and adult *A. muris* into the intestine of rats (*ibid.* 1936 v 33 583) and also (*ibid.*, 1936 v 33 120) surgically united the circulations of two rats infested with this species. Chandler's results show that work of this kind should compare the results obtained in normal and abnormal hosts and also those obtained with species whose larvae migrate through the body of the host, whether they penetrate the skin (*Aspistrostrongylus*) or not (e.g. *Ascaroidea*) and those whose larvae do not thus migrate.]

Vinsitzky found that the introduction of even large numbers of *A. lumbricoides* and *T. canis* did not so long as the nematodes were alive cause any important clinical symptoms in the cats, dogs and guinea pigs but when the nematodes were first killed, the experimental animals died, and when they were first "dissected," so that the peritoneum was liberated into the experimental animal, the death of the latter was very rapid. If however the animals were first immunized by previous introduction [presumably surgical introduction] of living ascars, they resisted repeated introductions of dead or "dissected" ones.

The two species of nematodes used lived in the animals for varying periods up to 10-12 days. They showed a tendency to leave their unaccustomed situation: they were able to bore into the intestinal lumen and in one instance perforated the stomach wall. Microscopical examination revealed blood in the intestine of ascars living in the peritoneal cavity. In guinea pigs the parasites were encapsuled, and phagocytosis followed, first by polymorphonuclear macrophages and later by mononuclear macrophages, both of which can penetrate the nematode cuticle and egg membrane. Probably these cells also secrete enzymes which help the process. Phagocytosis was at its maximum 33-35 days after the operation. In guinea pigs killed 57-62 days after it there was no trace of the parasites. In rabbits there was early encapsulation and multiple adhesions ["coalescences"] of the abdominal organs. An over abundant "exudation" of leucocytes slows up or completely stops the phagocytosis: the ascars are walled off by leucocytes but penetration into the cuticle, eggs or other organs of the nematodes was never seen. The nuclei of

the leucocytes showed karyolysis and karyorrhexis and, round the ascarids they were converted into a necrotic mass in which 47 days after the operation the ascarids and their eggs were still intact

In dogs and cats there was no encapsulation but very rapid lysis of the ascarids the rate of which varied with the number of nematodes introduced and with the response of individual animals. Usually lysis of 2-3 living ascarids was complete in 9-12 days. Into one cat weighing 2,800 gm. 31 *A. lumbricoides* measuring 20-30 cm. long were introduced and at autopsy 42 days after the operation, complete lysis had occurred. During the lysis and soon after its completion the peritoneal fluid of the cats contained large numbers of neutrophil polymorphs and monocytoïd cells and cells transitional to very large and active polymorphonuclear macrophages. Polymorphonuclear cells penetrated the ascarid cuticle and later the internal organs and also destroyed the eggs. No adhesions of abdominal organs were seen in carnivora. In hens there was no lysis and no phagocytosis the ascarids were simply mummified.

Thus the process was essentially the same in all the experimental animals and the author relates it to what happens in the normal life history of various nematodes e.g. when nematodes leave the intestine when the development of their migratory larvae is prevented by encapsulation, when encapsulation is a necessary phase in the life history or when mature species live normally in the peritoneal cavity and are encapsuled only when they are dead or dying. The response observed is essentially the same as that shown to a foreign body and to pathogenic agents in general namely immigration of phagocytes proliferation of connective tissue and encapsulation and after the isolation of the parasite destruction of it by phagocytosis. If it cannot be destroyed, the host either succumbs or host parasite adaptation develops in the course of evolution. Cats and dogs have however developed the ability to destroy these parasites. The author explains this by the view that in most animals encapsulation precedes phagocytosis or occurs simultaneously with it so that phagocytosis is greatly delayed or prevented but in carnivora the phagocytes have a maximum mobility and activity while encapsulation is delayed or eliminated. Probably this is not a special defensive reaction developed by carnivores to nematodes it is more likely that in the course of evolution the mesenchyme of carnivores has developed a phagocytic response which is more efficient than that of other animals.

G. Lapage

YU N G & MAO C. P. Preliminary Report of *Microfilaria malays* Infection in Chungking. *Chinese Med J* (Chengtu Edition) 1944 Apr v 62A No 3 114-20 2 charts [18 refs]

A Chinese man aged 18 was admitted to Chungking Municipal Hospital Szechwan Province in October 1943 because microfilariae had been found in his blood about two weeks before by a malaria unit. Observations on morphology and periodicity were made and are recorded in tables. It was impossible to determine when and where he became infected but he is stated to have lived in the neighbouring province of Hupeh for the first 11 years of his life i.e. until 1936 since then in Szechwan province and never to have been to other provinces. The microfilariae were most numerous at night reaching the maximum at 2 a.m.

J. F. Corson

BRADY F. J. LAWTON A. H. COWIE D. B. ANDREWS H. L. NESS A. T. & OGDEN G. E. Localization of Trivalent Radioactive Antimony following Intravenous Administration to Dogs Infected with *Dirofilaria immitis*. *Amer J Trop Med* 1945 Mar v 25 No 2 103-7 2 figs

CULBERTSON & ROSE [this Bulletin 1944 v 41 772 1945 v 42 136] used cotton rats infected with *Leishmosoides carini* in chemotherapeutic tests

on filariness with antimony compounds. This element is difficult to detect in small amount in tissues and fluids. GOODWIN and PAGE [this *Bulletin* 1944 v 41 20 222] have studied its excretion in laboratory animals, using a polarographic method. The present investigation deals with the distribution and fate of injected antimony compounds in dogs and it is hoped that the methods may serve as an aid in selecting new chemotherapeutic agents. After trying biological and spectrographic methods, without success radioactive antimony prepared with the aid of the cyclotron was employed. A technique was developed for locating the active substances in tissues by mounting thin sections on a photographic plate. Radioactive phosphorus had previously been used by McCoy *et al* (*J Parasitol Supplement* 1939 v 25 33 1941 v 27 53) in studies on encysted *Trichinella* larvae. The radioactive antimony was obtained as the trioxide and was then used in syntheses of tartar emetic and sodium antimonyl xythol. The degree of radioactivity in compounds and tissues was determined by means of Geiger Mueller counters with scaling circuits and also by the ionization chamber. Four dogs naturally infected with *Dirofilaria immitis* were treated intravenously with the three compounds and received 0.8 mgm. of antimony per kilo of body weight. Blood and urine were then collected at intervals up to 36 hours, when the animals were killed and residual urine and tissues were collected for determination of their radioactivity by comparison with standards. In the range 0.25-40 micrograms the accuracy of determination was very high. It was found that nearly all injected antimony had left the blood in a few hours. The liver contained the greatest concentration and next in order of content came the thyroid tissues. The adult worm on recovery contained about $\frac{1}{2}$ that in the liver. The lymph nodes and dermis, which are the chief sites of some adult human worms, contained very little antimony. After 36 hours the amount excreted in the urine varied from 10 to 20 per cent. of that injected. The fluid and tissue content of the element after injection of the insoluble trioxide was low.

J. D. Fulton

FRANCISCO RUIZ R. Datos para la exploración clínica del oncocercosis. [Clinical Findings in Onchocerciasis.] *Boletín Oficina Sanitaria Panamericana* 1944 Dec. v 23 No 12 1081-9. English summary.

Onchocerciasis common in Africa west and east but especially the former is found in the New World only in Guatemala and Mexico and in the latter of these in the States of Chiapas mainly and, to a less extent in Oaxaca.

This article is a general talk on the disease from the clinical aspect a sort of clinical lecture to students, telling them what questions to ask a patient regarding the history, place of residence, habits, occupation, what signs to look for such as tumours, eye lesions, laboratory examinations for eosinophilia and for filarial embryos in the skin. It contains nothing which is not familiar to readers of this *Bulletin*.

H. Harold Scott

DEFICIENCY DISEASES.

GILLMAN T & GILLMAN J. Methionine and the Fatty Liver of Infant Pellagrins. [Correspondence.] *Nature* 1945 May 26 634.

The authors have already described the syndrome of malignant infantile pellagra in South African children, and the dramatic cure which may be attained by treatment with ventriculin even when treatment with nicotinic acid or other vitamins has been unsuccessful [see this *Bulletin* 1944 v 41 1057]. One of

the most important features of this disease and one which gave the best criterion of the condition was the presence in the liver cells of large amounts of fat and the authors have devised an improved method of liver biopsy by means of which the progress of the disease can be studied. They tested the effect of methionine in two infants exhibiting the syndrome of malignant pellagra while a third infant with the same condition was studied as a control [it is known that small quantities of methionine decrease the liver fat content]. The condition of the liver at the beginning of treatment was similar in all three.

The infants were given maize porridge and half strength milk and methionine was administered orally—8 gm. in four days and 11 gm. in seven days in the two infants respectively—but had no beneficial effect. It was then stopped and treatment with ventriculin and a full diet was substituted recovery took place but was slow. The control infant received no treatment at first and was given the same porridge and milk but when ventriculin was administered rapid and uneventful recovery took place.

Under fluorescence microscopy there was no typical vitamin A fluorescence in the Kupffer cells but the fat droplets in the liver cells showed a dull greenish white fluorescence this does not imply that they will respond to methionine. It is evident that under these conditions methionine is not useful the best treatment remains the administration of ventriculin and a full diet.

Charles Wilcocks

PRILO J S Deficiência de ácido nicotínico em patologia humana (pellagra)
[Nicotinic Acid Deficiency in Pellagra.] *Brasil Medico* 1945 Jan. 6 & 13
v 19 No 1 & 2 4-13 7 figs. [30 refs.]

COPPING A M Some Aspects of Riboflavin Nutrition in Man. *Nutrition Abstracts and Reviews* 1945 Jan. v 14 No 3 433-40 [80 refs.]

A review of the literature which does not lend itself to abstraction. Most of the papers referred to have been reviewed in this *Bulletin*.

SPRUE

ISBISTER J A Case of Sprue Syndrome. *Med J Australia* 1945 Apr 14
v 1 No 15 371-4 4 figs [15 refs.]

This is a full and well documented account of a classical case of tropical sprue in a man of 32 from Cairns Queensland. The diagnosis was made on the following points—(a) general asthenia and emaciation (b) ulceration of the mouth (c) fatty diarrhoea (d) macrocytic anaemia (e) flat curve result of the oral glucose tolerance test (f) deficiency pattern of the small intestine and (g) course of the disease.

Special attention has been paid to the radiographic appearances of the small intestine. The *moulage* sign in the upper jejunum is so called because the opaque meal has the appearance of wax poured into a mould. This finding is diagnostic of steatorrhoea. Dilatation is present and segmentation in the more distal portions of the small intestine is shown by the clumping together of the barium in separate areas it is probably due to spasm.

P Manson Bahr

HAEMATOLOGY

TAYLOR G. F. & CHUTTANI P. N. Nutritional Macrocytic Anaemia and the Animal Protein of Diet. *Brit Med J* 1945 June 9 800-802.

Fifty consecutive unselected cases of anaemia were admitted to a hospital located in a hot desert climate serving a population of adult male Indians of whom 17 000 were meat-eaters and 1 188 vegetarians. The admission rate per 1,000 for anaemia was 22 times as great among the vegetarians as among the meat-eaters.

The anaemia also differed in type and severity in the two groups being mainly severe and macrocytic in the vegetarians but mild and hypochromic in the meat eating group. No case of nutritional macrocytic anaemia was seen in a meat eater while 24 cases of nutritional macrocytic anaemia occurred amongst the vegetarians.

Vegetarianism was thus thought to be the principal cause of nutritional macrocytic anaemia in this series.

L. J. Davis

DERMATOLOGY AND FUNGUS DISEASES

LEÓN BLANCO F. & OTEIZA A. The Experimental Transmission of Pinta, Mal del Pinto or Carate to the Rabbit. *Science* 1945 Mar 23 309-11

In Cuba one of the difficulties of studying mal del pinto is that pinta-like lesions can be produced by the spirochaete of syphilis. Several investigators have tried to infect laboratory animals with *Sp. herreyoni*, the causal agent of pinta, but with equivocal success. The importance therefore of this contribution is great.

A Jamaican negress showing the signs of pinta on palms and soles was seen by the authors and the organism was visible in material from the lesions. But this organism is not distinguishable morphologically from that of syphilis and the Kahn and Meinicke reactions are positive in both. To prove that the condition was pinta and not syphilis a volunteer was inoculated at two points on the front of the left forearm with fluid from the lesions. Primary pinta manifestations appeared here in course of time and there were when writing signs of general spread of pinta. Forty five days after the primary inoculation of the volunteer serous fluid squeezed from the initial lesion (which contained the spirochaetes) was diluted with normal saline and four rabbits were inoculated intradermally in the scrotum. Fifteen weeks later one of them presented a pink papule at the inoculation site which in another ten days became an erosion covered by a scab. From the base of this a bloody serum oozed containing numerous spirochaetes and four more rabbits were similarly inoculated from this. No lesions have as yet developed in these [the interval is not stated but from information gleaned from the text probably 54 days] but a volunteer inoculated at the same time as this second batch of rabbits developed a local inflammation which cleared in 72 hours but 13 days after the inoculation an erythema, 2 mm. in diameter was seen which ten days later became an infiltrated papule and in another month measured 6 by 4 mm. and had a fine scaly surface and many spirochaetes were seen in the expressed fluid. In the present state of our knowledge the only laboratory method which will allow with certainty to differentiate syphilis from pinta, mal del pinto or carate is the experimental inoculation of man with the production of an initial pinta lesion.

different from that of syphilis and plan [A method not altogether devoid of risk in a country where syphilitic lesions may simulate those of pinta.]

H Harold Scott

CLOUGH F E *Madura Foot. Western J Surgery Obstet & Gynecol* 1945 May
v 53 No 5 153-6 3 figs.

A report of a case.

HEAT STROKE AND ALLIED CONDITIONS

EICHNA, L. W BEAN W B ASHE W F & NELSON N *Performance in relation to Environmental Temperature, Reactions of Normal Young Men to Hot, Humid (Simulated Jungle) Environment. Bull Johns Hopkins Hosp* 1945 Jan v 76 No 1 25-53 19 charts [16 refs]

The physiological reactions were studied of 64 healthy young men who lived continuously in a hot room for periods of 8-32 days. During the day the men were exposed to an environment having a dry bulb temperature of 90°F with a relative humidity of about 95 per cent. At night the temperature was lowered to 85°F and the relative humidity to 75-80 per cent.

If the men were given progressively increasing work acclimatization to the heat was apparent on the second day of exposure and was complete in seven to ten days. Acclimatization resulted in the men being able to work with a lower heart rate lower skin and rectal temperature a more stable blood pressure and less discomfort than on the first day of exposure to the heat. Men resting in the heat for six to ten days achieved only a small degree of acclimatization as measured by their ability to work in the heat. Physically fit men were found to acclimatize more rapidly than unfit men and when acclimatized were capable of more efficient work. Initial intolerance to heat did not preclude rapid and complete acclimatization if adequate rest water and salt was provided. A considerable degree of cross acclimatization between desert and hot humid climates was demonstrated.

Adequate water intake was found to be the most important factor influencing the performance of acclimatized men in the heat with physical fitness next in importance but it should be pointed out that the effects of restricting the salt intake the effects of varying the severity of the work or of varying air movement were not studied. Restricting the water intake of acclimatized working men led to a marked deterioration in performance without reducing the rate of sweating. Clothing was found to increase the strain imposed by the hot humid environment though the deleterious effect was somewhat less if the clothing was wet. Other factors mentioned as adversely affecting performance in hot humid environments were inadequate sleep the taking of alcohol and long periods of work but no satisfactory data are presented concerning these points. Small changes in environmental temperature were found to have a marked effect on the physiological response.

One group of four men working in the humid heat during a continuous stay of 23 days developed a definite deterioration in performance after reaching the peak of their acclimatization. Their performance on returning to the heat after four days in cool conditions was as good as at the peak of acclimatization. An attempt to achieve a similar deterioration in 15 men who worked in the humid heat during a stay of 28 consecutive days resulted in failure.

The authors stress that sweating in humid heat is profuse, grossly inefficient wastes water and salt and is independent of fluid intake. Replacement of lost

water and salt is essential, but they point out that thirst is a lagging guide to these needs

A considerable number of charts illustrate the various points, but no tables of results are given.

B McArdle

BURCH G E A Method for measuring Small Amounts of Weight Loss in Man. *Amer J Med Sci* 1945 Feb v 209 No. 2 220-26 3 figs

A balance is described by which a human subject can be weighed with an accuracy of 0.150 gm. Changes of weight can be recorded photographically over short or long periods.

J Waterlow

BURCH G E & WINSOR, T The Relation of Total Insensible Loss of Weight to Water Loss from the Skin and Lungs of Human Subjects in a Subtropical Climate. *Amer J Med Sci* 1945 Feb v 209 No 2 228-34 1 fig [11 refs]

By means of the balance described measurements of insensible weight loss were made in normal human subjects. The room temperature was 75-82°F with a relative humidity of 30-60 per cent. Two methods were used to estimate separately the evaporative loss from the lungs and from the skin.

- (i) The subject breathed into a basal metabolism machine which was placed with him on the balance. The weight loss was then due only to evaporation from the skin.
- (ii) The subject was enclosed in an air tight cylinder which was placed on the balance. He breathed through a valve to the air. The weight loss was then due only to evaporation from the lungs.

The rate of total insensible loss was slightly greater in winter than in summer although the room temperature was kept the same.

At the environmental temperature used it was found that evaporation from the lungs accounted for 50-60 per cent of the total insensible loss of weight. There was no difference in weight loss between negroes and white subjects.

The rate of weight loss from corpses was rather less than the loss from the skin alone in living subjects. The authors reject the possible explanation, that some of the skin loss during life was caused by sweating. They consider that in both living and dead subjects, all the skin loss was by diffusion but that the rate of diffusion was higher during life because of a higher skin temperature.

J Waterlow

WINSOR, T & BURCH G E Differential Roles of Layers of Human Epigastrio Skin on Diffusion Rate of Water. *Arch Intern Med* 1944 Dec. v 74 No 6 428-36 12 figs

In dead skin when the epidermis was cut away the rate of diffusion of water through the dermis was found to be much greater than through the whole skin. In the living subject, when the superficial layers of epidermis were removed by blistering water passed through the remaining layers much more rapidly than through intact skin. On the other hand rate of passage through the epidermal sheet removed by blistering was the same as through normal skin. It was concluded that the barrier to free passage of water lies in the stratum corneum.

J Waterlow

BURCH G E & WINSOR, T Rate of Insensible Perspiration (Diffusion of Water) locally through Living and through Dead Human Skin. *Arch Intern. Med.* 1944 Dec. v 74 No 6 437-44 9 figs [10 refs]

A method is described for measuring the rate of loss of water from the skin. A brass cup is sealed to the skin and oxygen circulated through it. The water vapour taken up is condensed and weighed.

The rate of diffusion through dead skin was measured by suspending the skin with a brass cup attached in a bath of saline. When comparisons were made between living and dead skin the temperature of the saline was adjusted to equal the skin temperature of the living subjects.

At a room temperature of 75°F and 50 per cent relative humidity the rates of loss from living and dead skin were essentially the same. At 115 F and 80 per cent relative humidity the rate of loss from dead skin increased only slightly whereas from living skin it increased fourfold. The authors conclude that at the lower temperatures all the water lost from the surface of living skin had passed through the skin by diffusion. The increased rate of loss at the higher temperature was caused by sweating. Since the rate of diffusion through dead skin was not changed when the skin was kept for three or four weeks in a refrigerator and frozen and thawed several times during that period it is suggested that the barrier to free passage of water lies in some non living structure.

J. Waterlow

MISCELLANEOUS DISEASES

MARRIOTT H. L. Medical Problems of South-East Asia Command. *Lancet* 1945 June 2, 679-84

This paper is packed with valuable information and suggestions and as the author states a comprehensive review such as this does not lend itself to summarising. A few points from the paper follow.

Although the British and Indian troops of the S.E.A.C. are in first-class physical condition and of excellent morale there is an enormous wastage of man days through sickness which is not of a serious nature. One medical officer engaged in hygiene can save the work of ten medical officers in hospitals. Education of the troops is essential and a special propaganda section would be of great value.

Malaria is the greatest problem. It has caused half of the sickness but its incidence is only a fraction of what it was. For security reasons it is not permissible to report in detail the measures by which this success has been gained.

The present standard treatment for British soldiers is 0.3 gm. mepacrine thrice daily for the first day, 0.2 gm. thrice daily on the second day and 0.1 gm. thrice daily for five days. It is the same for Indian soldiers except that on the first day 0.2 gm. is given thrice daily.

Benign-tertian relapses are frequent but are not of great importance.

In the treatment of cerebral malaria the Fowler position is adopted and a nasal tube is used to maintain a constant drip into the stomach to combat dehydration.

Diarrhoea and dysentery are next in importance. Diagnosis in the past has necessarily been rough and ready. In 20 per cent. of the cases *Entamoeba histolytica* has been found, the rest of the cases have been assumed to be bacillary and their response to sulphonamides has been prompt in the vast majority of instances. When these drugs fail to cure within five days a thorough investigation is carried out, and when amoebic infection is diagnosed the treatment is on standard lines. The routine treatment of all known and suspected cases of bacillary dysentery by sulphaguanidine is believed to be of great value in preventing the spread of infection.

Scrub typhus in 1944 attacked one man in every hundred exposed to risk. The case fatality rate was 10 per cent. The patients must not be transferred

after the first few days. The essential points in treatment are skilled nursing, a cool ward, maintenance of fluid and salt balance, adequate nutrition and oxygen at the onset of cyanosis. Very energetic preventive measures are in train.

One outbreak of infective hepatitis was suspected of having been caused by an infected syringe used in giving cholera vaccine.

The chief causes of "heat effects" were dehydration and salt depletion. Salt should be added to the drinking water at the rate of 3 gm. per litre.

Dehydration plays an important part in every serious medical and surgical illness in the tropics. The urinary output should be measured and tested for its salt content every eight hours. A simple test is by placing ten drops of urine in a test tube, adding one drop of a 20 per cent solution of potassium chromate, and then adding with constant shaking and drop by drop a 2-9 per cent solution of silver nitrate. The number of drops needed to change the colour from yellow to brown gives the number of grammes of sodium chloride in each litre of the urine. An eight-hourly output of over 15 oz. and a salt content of 6-12 gm. per litre are aimed at.

A sprue-like condition, occurring in both British and Indian troops, is regarded as due to malnutrition caused by the vicious circle—diarrhoea—resulting failure of absorption—deficiency of the vitamin-B complex—diarrhoea due to this deficiency. Special vitamin tablets are issued to all the troops but these do not obviate the need for a generous diet. The treatment is directed first to the original causal factors such as dysentery and malaria. A high-protein, high-vitamin and low-fat diet is given. To this are added six compound vitamin tablets and 3 oz. marmite or similar preparation daily. Injections of liver extract, nicotinic acid (100 mgm. daily) and riboflavin (10 mgm. daily) are also given.

Anaemias are more prevalent among Indian than British troops probably because most of the Indians elect to take milk instead of meat in their ration.

John W. D. Megaw

PATEL, N. D. Benign Eosinophilia with Pulmonary Shadows. *Indian Physician* 1945 May v 4 No 5 93-109 3 text figs. & 8 figs. on 2 pls. [30 refs.]

An excellent account of the main features of this interesting symptom complex about which so much has been written recently. The author's remarks are based on a study of 49 cases under his personal observation during a period of 14 months. The disease is clearly far from uncommon if one practitioner can see so many in so short a time. Forty-seven were from Bombay Province, 37 were males, 12 females but since males preponderate among those seeking medical advice this is no proof that the disease is really more common in them. The ages ranged between 8 and 56 years and the leucocyte counts up to 29,000 with 81 per cent eosinophiles, 38,500 with 74 per cent and 42,350 with 68 per cent eosinophiles. No place in the aetiology could be assigned to occupation, social status, food habits, smoking or alcohol. Some who have studied this condition have emphasized the fact of there being no familial susceptibility nor other cases of allergy in the family of one affected, but the author's experience does not bear this out. Others WEINGARTEN for example [*this Bulletin* 1943, v 40 407-1944 v 41 424] have observed that arsenic brings about complete cure and thus relapses do not occur. Dr. Patel records the case of a patient with two relapses each after an interval of 3½ years and a third 23 months after the second. He stresses the importance of making blood examinations and X-ray examination of the chest in all cases of chronic cough with a history of asthmatic attacks and loss of weight. He notes, as others have done, the recrudescence of the subjective symptoms and the leucocytosis and eosinophilia in the early stages of arsenical treatment whether by injection or *per os*.

As regards the pathology and pathogenesis he thinks it is allergic and that the pulmonary interstitial tissue is sensitive rather than the bronchi (as in ordinary asthma) on the ground that the infiltration is largely in and around the alveoli. [The paper was read at a medical meeting and several took part in the subsequent discussion but added nothing fresh most of them relating cases in their own experience.]

H Harold Scott

RANDALL, T Eosinophilic Pneumonitis (Loeffler's Syndrome) with Response to Emetine. *Brit J Tuberculosis* 1945 Jan v 39 No 1 37-8

A coloured man, aged 20 was admitted to a hospital in Durban, Natal complaining of substernal pain of one month's duration and of severe cough with copious expectoration (occasionally blood-stained) for two weeks.

Examination of the chest showed increased vocal fremitus and vocal resonance in the upper third of the right lung and crepitations in the right apex and mid zone. A radiograph presented the appearances of tuberculous infiltration of both lungs more marked on the right side where there were several sizable areas of apparent excavation. Eight successive examinations of the sputum showed no tubercle bacilli nor were amoebae or fungi found. The faeces were normal. A blood examination showed haemoglobin 14.2 gm per cent erythrocytes 4.3 millions per cmm colour index 1.1 leucocytes 9,600 with neutrophils 74 per cent eosinophiles 6 per cent large mononuclears 1 per cent. and lymphocytes 19 per cent.

His temperature which had been between 99 and 100.4°F since admission became normal after six days in hospital but his condition was otherwise unchanged. Emetine 1 grain daily for 10 days was given intramuscularly and dramatic improvement followed all symptoms disappearing rapidly. A radiograph of the chest showed no abnormality. He was discharged cured.

The author states that there was no evidence of amoebiasis except the eosinophilia, the prevalence of amoebiasis in Durban and the quick recovery after the course of emetine. He refers to papers by DORMER and FRIEDLANDER [this *Bulletin* 1942 v 39 31] and by HOFF and HICKS [*ibid* 1942 v 39 792]. [Eosinophilia is probably not evidence of amoebiasis see comment on DORMER and FRIEDLANDER's paper in this *Bulletin* loc cit.] J F Corson

McFARLANE A. L. & BRANDAY W. J. Hepatic Enlargement with Ascites in Children. *Brit Med J* 1945 June 16 838-40

[Any contribution which may help to throw light on cirrhosis of the liver of obscure aetiology is welcome. Many papers have been written on it but the conclusions reached are meagre and the results show a poor return for all the work which has been done on it [see this *Bulletin* 1938 v 35 909 (a careful consideration of the whole problem) 1942 v 39 415 1943 v 40 333]. The International Commission for Geographical Pathology has made it a subject of special study (see STITT's *Tropical Diseases*, 6th ed. 1942 1594 and other textbooks of Tropical Medicine).]

The authors give a brief account of 18 cases in children between one and ten years of age under their observation in a single year in Kingston, Jamaica. Two have died the disease is usually chronic lasting for months or even years affects children and ends in recovery in the majority of cases. The condition in Jamaica would seem therefore to differ radically from that seen in India and the Far East where the fatality rate is high and some run an acute course. The symptoms are however similar in many respects early fever anorexia nausea vomiting abdominal enlargement hepatomegaly (the liver may extend to the umbilicus and even lower) ascites little or no jaundice. Splenic enlargement

was seen in less than half the cases. The Kahn reaction is negative (in 14 out of 15 of the authors' patients) [but a positive Kahn is of little significance in a place like Jamaica where yaws is common in children]. The blood shows "moderate anaemia" and "moderate leucocytosis." [No figures are given, which is a pity: as more elaborate laboratory procedures were carried out such as van den Bergh reactions, sedimentation rates, fragility tests, estimations of blood urea and sugar. All but the first of these were normal.]

In the single autopsy performed the liver showed a pericellular type of cirrhosis "resembling Hanot's cirrhosis." [Histologically this is correct but clinically Hanot's cirrhosis is characterized by hypertrophic cirrhosis with icterus and without ascites: whereas in the authors' cases there was ascites with little, if any jaundice.]

The authors incline to the view that a dietary deficiency may be the primary cause: as in these patients the diet is inadequate and unbalanced, often irritant, and improvement followed change of diet alone and the same with administration of glycocholl. Dried yeast also benefited "a small number of cases."

[Since as many as 18 cases came under the authors' observation in one town in one year opportunities should not be wanting for a deeper study of these interesting cases. Nothing is said of faecal examinations or of helminthic infestation nor whether similar cases occur elsewhere in the island. This would seem to be a good opportunity for useful research on a subject of wide interest to the east as well as to the west.]

H. Harold Scott.

EAST AFRICAN MED J 1945 Apr. v. 22, No. 4 126-7 A Case of Stramonium Poisoning.

The author of this note himself suffered from symptoms, strongly suggesting stramonium poisoning after eating bread. The gram came from a farmer who admitted that his farm was full of stramonium, but under the circumstances the bread could not be examined. Proof is therefore not conclusive [but in view of this and other reports from East Africa, it seems that the possibility should be borne in mind. The author does not say in what area the incident occurred.]

Charles Wilcocks

KAO Yung En & CHEN Shui-Chao. A Clinical Study of Ginkgo-Nut Poisoning among Children in Kweichow. Report of 7 Cases. *Chinese Med J* (Chengtu Edition) 1944 Jan. v. 62A No. 2, 64-6

Ginkgo nuts (*Ginkgo biloba* L.) are grown and eaten by adults in South China. For some reason, perhaps because they are known at times to cause toxic symptoms, children under ten years of age are not allowed to eat them in Kweichow for example. The nut does not seem to be, as a rule, very poisonous, for a case is recorded of poisoning after ingestion of 1 000 of them: their toxicity would, however, appear to vary for of the seven cases recorded here a child aged 4 years died after eating 150, another aged 7 months died after taking seven, while others whose ages ranged from 14 months to 2 years ate from 30 to 50 and recovered. The chief symptoms are restlessness followed by convulsions, 1-9 hours after eating the nuts, abdominal distension, dyspnoea, delayed or lost light reflexes, unequal pupils and unconsciousness. There is usually some fever to 40 C. with leucocytosis from 14 000 to 21 000 or more (the infant of 7 months who died had 50 000 per cmm).

B. E. READ in a work on Chinese Foods gives the following as the composition of the nuts. The figures taken from Neil LITCH's work on *Dietetics in Warm Countries* (p. 280) are also given for comparison, since the differences are considerable. The first set are for nuts as purchased, the second are those for the edible portion.

	Protein	Fat	Carbohydrate	Crude fibre	Ash
Read	8.48	2.46	37.75	0.30	1.32
Leitch	13.4	3.0	71.2	0.5	2.8
	9.0	2.0	47.8	0.3	1.9

The authors state that CHU reported in July 1943 on the chemistry and toxicology of these nuts but say also that the actual toxic constituent is not known to them. [Work on this might be advantageously undertaken for it is clearly a useful food (the calorie value of the edible portion is given by Leitch as 365 per 100 gm. or 2.044 per catty) but is nevertheless at times dangerous.]

H. Harold Scott

GENERAL ENTOMOLOGY

CRANDLER, A. C. Factors influencing the Uneven Distribution of *Aedes aegypti* in Texas Cities. *Amer J Trop Med* 1945 Mar v 25 No 2, 145-9

The author gives an interesting account of the spread of the ubiquitous *Aedes aegypti* in the United States. The following is quoted from the summary.

The prevalence of *Aedes aegypti* in early summer in Texas cities is very variable. Only in the Lower Rio Grande Valley is the winter climate mild enough to allow this mosquito to survive without protected hold-over places in sufficient numbers to produce a high incidence of breeding early in the season every year. In other cities early prevalence of breeding is associated with abundance of protected winter hold-over places especially cisterns, fire-protection barrels in compresses and warehouses or shallow wells. In cities having only a few such hold-over places a high breeding index does not develop until late summer and in many smaller cities such an index may not develop at all unless the mosquitoes are imported from elsewhere in automobiles or freight cars. In such cities the occurrence and prevalence of *Aedes aegypti* may vary from year to year depending on whether or not such an importation occurs early in the season. In coastal cities alternation of cold and warm periods during the winter has a harmful effect on the survival of *Aedes aegypti* and may be more important in holding the insect in check than the extremes of cold or the total amount of cold weather.

R. M. Gordon

PUBLIC HEALTH REP. Wash. 1945 Apr 27 v 60 No 17 469-70 Use of DDT for Mosquito Control in the United States. A Joint Statement of Policy by the United States Army and the United States Public Health Service

The great success which has attended the use of DDT in combating insect borne diseases during the war has fostered a hasty conclusion that it is a complete solution to all problems to which insects give rise. In this short statement however a warning is given that DDT distributed over the countryside not only destroys mosquitoes but may also kill many insects which are biologically beneficial. Much remains to be learned about the effect of DDT on the balance of nature before its general outdoor application can safely be instituted.

Extensive investigations are in hand to obtain this information but in the meantime the joint policy of the United States Army and the United States Public Health Service is laid down in the following paragraphs —

1 DDT will be used for residual spray application to houses and other buildings for the purpose of killing adult mosquitoes before they have opportunity

the rice fly. It breeds in pig manure unlike *C. megacephala* which breeds in liquid human faeces and haunts insanitary latrines of which there are many thousands in Chengtu. It seems that flies may transmit *Ascaris* and *Trichuris* but these, being transmitted much more efficiently by other means are probably not important in this connexion. In the transmission of *E. histolytica* and its associated protozoa, however flies may play an important part.

Charles Wilcocks

VANDERPLANK, F. L. Apparent Densities of certain African Blood-Sucking Insects (Diptera). *Proc Roy Ent. Soc London* 1944 v 19 Pt. 4-6 68-72. [Summary taken from *Rev Applied Entom.* Ser B 1945 May v 33 Pt. 5 83]

Tabanus and *Glossina* spp. were collected on 1-11 days in each month from November 1940 to August 1941 on a tethered ox in a hardpan area near Old Shinyanga in Tanganyika Territory. The ox was being used for attracting *Glossina*. Tables show total monthly catches and mean monthly catches for a specified period of both sexes of *Glossina swynnertoni* Aust. and *G. pallidipes* Aust. and of females of *Nuceria neavei* Aust. three species of *Tabanus* two of *Pangonius* three of *Dorcaloemus* and unidentified species of *Haematopota*. Data are also given on the monthly rainfall and mean maximum and minimum screen temperatures. The catching site and methods used are described. *Tabanus* and *Haematopota* were caught in most rainy months but *Pangonius*, *Nuceria* and *Dorcaloemus* only during April and May towards the end of the rains. *G. pallidipes* decreased in numbers from November to December and then gradually increased. *G. swynnertoni* increased during the rains and decreased during the dry season. *Tabanus* was active towards mid-day when *Haematopota* was inactive except on cloudy days. *Pangonius* was most active at mid-day and during the afternoon. *P. zonatus* Wlk. was taken in extremely large numbers during April, and it is suggested that it may be a factor contributing to the high incidence of trypanosomes in game at that period.

BISHOP, F. C. & TREMBLEY, Helen L. Distribution and Hosts of certain North American Ticks. *J Parasitology* 1945 Feb v 31 No 1 1-54 18 figs. [Numerous refs.]

In this paper the distribution of some 31 species of North American ticks is mapped from records compiled at the Bureau of Entomology and Plant Quarantine. Full lists are given of the hosts and the numbers of ticks of each stage collected from them. This throws an interesting light on the question of host specificity for although the host list for each species is often extensive relatively few appear to serve as major hosts.

Notes are also included on seasonal activity, the site of attachment to the host and the medical importance of the ticks. The latter summarizes what is known of each species as a disease carrier. Apart from this, however, the willingness of certain species to attach to man may constitute a source of considerable annoyance.

A. D. Lees

MISCELLANEOUS

COLONIAL OFFICE. Report of the West Indian Conference held in Barbados 21st-30th March, 1944 [STOCKDALE, F. Chairman] Colonial No 187 pp vi+21 1944 London H.M. Stationery Office. [6d]

The Conference was held in Barbados from March 21st to 30th 1944 and the Report is dated March 30th 1944. It comprised representatives of the following

local Governments¹—Bahamas Barbados British Guiana British Honduras Jamaica Leeward Island Porto Rico Trinidad, Virgin Islands of the United States and Windward Islands together with representatives of the Anglo-American Caribbean Commission (with United States and British Sections) and its advisory body the Caribbean Research Council.

In the Introduction a short history of the development of the Conference is given in 1943 the British and United States Governments agreed to collaborate for the improvement of social and economic conditions in the Caribbean area and established the Anglo-American Caribbean Commission more recently the Caribbean Research Council was formed as an advisory body to the Commission for the co-ordination of scientific and technical work.

The next step was to provide for consultations with local representatives official and non-official of the territories concerned, by establishing a series of West Indian Conferences under the auspices of the Anglo-American Caribbean Commission. The Conference will be a standing body with a central secretariat and will meet from time to time to consider special subjects. Each British or United States territory may send two delegates accompanied by advisers. The Conference will be purely advisory and have no executive powers unless such are specially entrusted to it by Governments. Other countries may be invited to participate on occasions.

While recognizing the existence of many other problems which will require and receive attention it was decided at this first session of the Conference to restrict discussion to the following subjects 1.—Means for raising the nutritional level ((a) local food production (b) expansion of fisheries) 2.—Re-absorption into civil life of persons engaged in war employment 3.—Planning of public works for the improvement of agriculture education housing and public health 4.—Health protection and quarantine 5.—Industrial development 6.—The Caribbean Research Council—possibilities for expansion.

Committees were appointed to consider and report on these items and their reports of which there are seven form the main contents of the present Conference Report.

I Item 1(a)—Greater local production and use of protective foods—meat milk and dairy products legumes eggs fruit and leafy vegetables—as required. It must depend largely upon remunerative returns from the export of staple crops.

Considerable improvement in the conditions of rural living is needed, viz increased income better water supply light and power education and medicine housing etc.

The Committee made detailed recommendations some of which refer to action by the Governments concerned and include the acquirement of land, provision of suitable conditions of land tenure by small settlers processing and storage of food, provision of assured food markets at suitable prices agricultural credit agencies purchase and sale of basic foodstuffs by Government supply of seeds implements and livestock educational food propaganda provision of milk for infants and lunches for school children food research must be intensified.

II Item 1(b)—The fishing industry should be expanded the means will vary in different territories. Among subjects to be considered for development are shark crawfish and shrimp fishing freshwater fishing sport fishing and the tourist trade marketing and distributing price control, welfare measures among the fishing population. The need for research on methods of capture handling and preservation of fish as well as fundamental research is strongly urged. The Committee gave a list of recommendations including the continued support of the Anglo-American Caribbean Commission.

III Item 2.—The Committee recommended that members of the Services should be allowed to remain in the Services for at least six months after

Dr Headlee shows that the victories which resulted in reducing the mosquito incidence in New Jersey depended on the studies previously made of the life histories and habits of the local mosquitoes. Thirty-one species are considered in the book and the bionomics of each of these species, together with the methods to be employed for recognizing their larval and adult stages are discussed in detail and occupy nearly two-thirds of the volume. In the space remaining at his disposal, Dr Headlee gives an account of how the knowledge gained from these studies has been utilized to devise anti-mosquito measures against both larvae and adults and adds an account of the laws which have been enacted to give force to these measures. The first of these was passed in 1902 and reads

BE IT ENACTED by the Senate and General Assembly of the State of New Jersey

1 The New Jersey Agricultural Experiment Station be and the same is hereby empowered and directed to investigate and report upon the mosquitoes occurring within the state their habits life history breeding places relation to malarial, and other diseases the injury caused by them to the agricultural, sanitary and other interests of the state their natural enemies and the best methods of lessening, controlling or other wise diminishing the numbers injury or detrimental effect upon the agricultural, sanitary, and other interests of the state.

This is indeed an enlightened document when compared with the difficulties encountered by Ross in his campaign in the British Empire.

The book concludes with an interesting chapter on the economic effect of mosquito reduction which shows the annual tax value increase in areas in New Jersey with and without progressive mosquito control. These figures of financial improvements are very convincing and the reviewer wonders whether similar figures could not be made available in Britain to show the remarkable effects which have followed Mr Marshall's successful work on Hayling Island.

The systematist will find this book of only local interest but those who are interested in the history of entomological research and its practical application to human problems will find much fascinating reading and from a study of its pages can forge a trustworthy weapon to defend the view that entomological research is the concern of the state as well as of the individual.

R M Gordon.

TRESTON M L. [C.B.E. F.R.C.S. F.R.CO.G. L.M.S. Inspector-General of Civil Hospitals Burma] *Health Notes for Government Officials.* 64 pp. with Appendices 8 folding plans & 3 figs. Published by the Director of Public Relations Government of Burma [n.d. n.p.]

During the present century there have been many medical men who have turned their attention to the exposition of medical knowledge for the benefit and instruction of the public. This is a tendency to be encouraged, since the argument in favour of popular understanding of the basic facts of certain diseases (especially the transmissible diseases and the deficiency states) is very strong but the technique of presentation needs careful thought and study. Too often, booklets of this kind give the impression of uncritical haste in the writing and of an insufficiently considered plan of presentation the result, usually is a series of brief chapters of dogmatic statements without sufficient explanatory matter to create in the mind of a non medical reader a satisfactory grasp of the elements of disease causation and transmission. To the reviewer it seems that any book of this kind which fails to explain the nature and effects of bacteria, protozoa and other parasites must largely fail in its object.

The small book by Colonel Treston is not an exception in this respect. Two examples may be taken to illustrate the point. On page 3 the remark is made

Have anyone who handles food or utensils *tested* to make sure that he is not a carrier but up to that point no explanation has been given as to what a carrier is or what in this connexion he may be carrying. Later the malaria parasite is mentioned but not explained or described. Other instances can be found.

This is not the only criticism which may be made against the book. There are inaccuracies which can hardly be excused. For instance Infection with worms is nearly always through an abrasion in the skin (p 15) shop typhus is transmitted by the bed bug the flea and the tick (p 23) fleas have a jumping range of 2 feet and carry two stings the one in the tail transmits plague typhus and relapsing fever (p 32) bugs are credited with carrying Typhus and Kala Azar (p 34) The advice given on page 7 that 'one tablet of Mepacrine Hydrochloride (Atabrin) 0.1 grm i.e. $1\frac{1}{2}$ grains twice weekly on two successive nights is of value in prevention of attacks of malaria conflicts with general experience and with the careful work done by FAIRLEY [this *Bulletin* 1945 v 42 656] such small dosage can hardly be useful in suppression and may lead to trouble by giving a false sense of security or by masking the disease.

These criticisms are valid but that does not mean that much of the advice given is not correct. Nevertheless it seems to the reviewer that those who write books of this kind should consider very deeply the methods they adopt of presenting the subject to non medical readers and that they should be at pains to ensure accuracy.

The author has included plans for layout of a small town for the construction of a well a bored hole latrine and a slaughterhouse and a table of daily food requirements calculated for Burmans.

Charles Wilcocks

MEDICAL CLINICS OF NORTH AMERICA. 1944 Philadelphia Number 1293-553 numerous figs. & charts Symposium on Recent Advances in Medicine [Reprinted by the U.S. Office of War Information from the *Med Clinics of North America* for November 1944]

This symposium is reprinted by the United States Office of War Information from *The Medical Clinics of North America* for November 1944 no doubt because the authorities recognize the value of brief papers which bring together the important new facts of medicine for those readers who have neither the leisure nor the opportunity themselves to read all the relevant literature as it appears in the medical journals. This function is well performed in the Symposium. The first half deals with recent work on Air Sanitation Otolaryngology Cardiovascular Disease Gastro-enterology Thyrotoxicosis Leukaemia Pituitary Myxoedema Rabies Acute Respiratory Infections and Fluorine. The second half from the Pennsylvania Hospital Overseas is concerned with certain subjects more allied to the contents of this *Bulletin*. A general account of immunity pathology and clinical manifestations in malaria is given by VANDER VEER and HEDBLOM which is useful in that it stresses the importance of malaria in tropical warfare and the need to be constantly watchful for pernicious symptoms. Laboratory diagnosis in malaria is summed up by DEWHOFF. The clinical aspects of scrub typhus are dealt with in the form of a comment on a case by DUNCAN and there is a fairly full account of dengue by EWING. McCLENAHAN gives a short account of leprosy and its relation to soldiers mixing with a population in which it is endemic, and HAINES and FORCEY an account of 40 cases of primary atypical pneumonia in troops in the South Pacific. The dysenteries are briefly discussed by CALARCO.

The remaining papers are concerned with Anxiety Neuroses Fractional Gastric Analysis and Thyroid Disease but there is also a useful paper on the

treatment of common skin diseases in the tropics—epidermophytosis, dermatitis venenata and bites by insects and mites which deserves attention

The publication is well produced and printed.

Charles Wilcocks.

HUNT Virginia Lloyd. *How to Live in the Tropics.* pp. ix+178 1942.
New York Harcourt Brace & Company [12s. 6d.]

This useful book written for non-medical persons, contains chapters on Preparations, Climate Environment, Daily Routine Food and Drink, Hobbies Women and Children, Insects Communicable Diseases Home Nursing and First Aid. It is attractively written and the advice given is sound. It can be recommended to intending travellers to the tropics.

Charles Wilcocks

TROPICAL DISEASES BULLETIN.

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[No 10

SUMMARY OF RECENT ABSTRACTS *

VIII TYPHUS GROUP OF FEVERS

Proteus OX19 type *Vectors* *louse and flea**Louse typhus*

An important contribution to the understanding of the epidemiology of louse-borne typhus has been made by PSHENICHNOV (p 836). There is no evidence that infection is transmitted hereditarily in lice but there is strong evidence that lice may acquire infection from infected louse faeces which contain masses of rickettsiae from the 3rd to the 17th day after the infecting feed. Louse faeces remain infective for only a short period on the human skin and under conditions of high humidity and warmth but when dry the faeces may be infective for several weeks or months especially at low temperatures. Human clothing therefore may remain infective and particles of infective faeces may be introduced on to the conjunctiva or other mucous membranes by the fingers or nails. Some methods used for the disinfection of clothing are not adequate for the destruction of rickettsiae.

In the *BoI Oficina Sanitaria Panamericana* (p 834) there is a report on the incidence of fevers of the typhus group in Latin America. MAGALHÃES (p 843) describes the rickettsial diseases of Brazil where tick typhus has existed for many years epidemic and murine typhus are also found.

GEAR *et al* (p 739) have reported on the extensive epidemic of louse-borne typhus which has existed since 1941 in the Transkei and which has been aggravated by the poor nutritional condition of the population. They have established the fact that the disease is not of murine origin, and that the symptoms are those usually found in other countries the rickettsiae isolated have also been shown to be unexceptional. An alum precipitated vaccine gave promise of success.

An epidemiological survey of typhus in Egypt since 1905 has been made by KAMAL and MESSIH (p 380) who state that it is much more prevalent in Lower than in Upper Egypt and that its incidence is chiefly in the rural population. Spread has been associated especially with the congregation of labour forces and their return home the winter and spring seasonal prevalence is well marked. During the war the incidence has increased, but this increase did not

*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1944 v 41. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

take place before workmen were recruited from Upper Egypt. In an account of the clinical features of a large number of cases of typhus in Egypt the same authors (p. 382) note that the fatality rate as is usual was low in early life and high at ages over 55. There was great variation in the type and severity of the symptoms in the different local outbreaks—the rash was present in only 32 per cent. in one outbreak, but in 85 per cent. in another. For details of other symptoms and of complications the original abstract should be consulted. The Weil-Felix reaction remained negative at the end of the third week in 14 per cent. of cases, and the authors do not regard this reaction as absolutely diagnostic unless the titre rises to 1-500—a skin test with killed *Proteus OX19* is said to be of value. There was no evidence of the existence of "mapparent" cases, or that any outbreak originated from flea-borne typhus.

BROCKBANK and WHITTAKER (p. 383) report 10 cases of typhus in British soldiers who had been in contact with Egyptian labourers—in 6 the diagnosis was confirmed by the rickettsia agglutination test. The authors point out the difficulty of diagnosis in sporadic cases. In an account of the clinical features of typhus in British troops in the Middle East, CROFTON and DICK (p. 1012) emphasize the variability of the disease. Many of their cases were of murine origin, the differentiation from the epidemic type being made by the rickettsia agglutination test—these murine cases were on the whole less severe than the others, but could not be differentiated solely on clinical grounds.

MCCOWN (p. 111) gives an account of an epidemic of typhus in Ireland. The disease was not at first suspected, and diagnoses of bronchopneumonia and influenza were made though rashes were found when looked for. Two other outbreaks are also mentioned—all occurred in Galway. The results of rickettsia agglutination tests on some of these patients, and carried out by STUART HARRIS *et al.* (p. 111) suggest that some at least of the patients had been infected with *Rickettsia prowazekii*. The findings give presumptive evidence that human cases of typhus can be classified as murine or epidemic by rickettsial tests.

SANCHEZ LOBO (p. 555) refers to an outbreak of typhus in Córdoba and notes that, as so often happens, the first cases were missed, being mistaken for influenza.

KUDICKE (p. 680) believes that the apparent infrequency of typhus in young children is not due to immunity against infection but to resistance by which the attack is modified. Children are attacked as often as adults but there are more mild infections, often missed. It is not known how far the blood, in these mild attacks is infective for lice. Records of the epidemic of typhus in Leningrad during the siege also show that children have no special resistance to actual infection, but that the disease is less severe in them than in adults. TOKAREVICH (p. 1017) also demonstrates that the incidence in children in Leningrad was relatively high.

BREYDO (p. 690) in discussing the difficulty of early diagnosis in typhus, draws attention to the appearance of a few single haemorrhagic areas in the region of the sacrum or buttocks, or near the scapulae. These may be seen 24 hours before the typical rash and are due to early trauma of the tissues through lying on the back. By observing them, diagnosis may be made on the third or fourth day but they may also be seen in scurvy or other haemorrhagic diseases. YALUFF and VERDAGUER (p. 385) refer to minute white spots which may be seen along the retinal vessels in typhus. These are said to be absolutely diagnostic and have been seen in 80 per cent. of one series of cases. AVTSIN (p. 201) describes petechial haemorrhages of the conjunctiva in typhus. These are not often seen in life, but may be found after death in persons who have died late in the disease or as a result of some complication. Their significance is that they justify a diagnosis of typhus even in the absence of clinical information.

RAETTIG (p 932) has studied the blood sedimentation rate in typhus there is much variation

CUMINO (p 26) has found electrocardiographic evidence of damage to the heart in every case studied in the febrile stage of typhus and in almost every one in the post febrile stage. Details of the findings are given in the original abstract. The necessity for avoiding effort during convalescence from typhus is emphasized by KUHLMANN and HEINRICH (p 932) as a result of their electrocardiographic studies.

KILLIAN and OBERTREIS (p 662) discuss the surgical complications of typhus. These are of two main types non-specific septic conditions and the results of the true typhus lesions of blood vessels chiefly the small arteries. These are discussed in considerable detail, for which the original abstract should be consulted. The authors note also that during the war in Russia typhus was common as a complication of surgical conditions. In these circumstances diagnosis can be very difficult.

SEIFERTH (p 933) notes that the majority of patients with typhus have ear symptoms usually with deafness which is ascribed to a central cause but of which the prognosis is generally good. Otitis media is not uncommon.

v STOCKERT (p 201) gives a list of the mental disturbances which may occur as a result of typhus

SEGAL and ZASOVA (p 386) point out that second attacks of typhus are by no means rare immunity in man is far from absolute. Second attacks tend to be milder than first, and the cardiovascular and nervous systems are less frequently affected.

BENHAMOU *et al* (p 25) have with difficulty been able to infect mice by the respiratory route with material taken by sternal puncture from patients with typhus.

SECRET (p 661) maintains that typhus can be aborted with certainty by the use of convalescent whole blood if this is given within one or two days of the onset. In comment MEGAW remarks that it would not be safe to assume that the blood of persons in the 8th or 9th day of convalescence is always free from infectivity [KILLIAN and OBERTREIS (above) make the point that blood may be infective up to 8 days after defervescence] BUHLER (p 742) writes favourably of the therapeutic effect of convalescent blood especially if it is given in the early stages of the disease the blood was taken from young healthy donors not more than 14 days after defervescence

PFEFFER and GAUWERKY (p 274) have treated 50 typhus patients with convalescent serum and compared the results with 100 controls. There seemed to be some indication of benefit from this treatment, as regards fatality rate length of fever and incidence of complications but the differences between the two series are slight. ALWENS and FRANK (p 274) have been favourably impressed by the results of treatment with convalescent serum, but the evidence on which they base their claims is not given in sufficient detail to permit evaluation. RAETTIG (p 275) also reports success with convalescent serum and injections of the patients own blood, but again the evidence given is poor. MEYER (p 115) quotes evidence which indicates that convalescent serum administered on the second or third day of an attack of typhus has some effect in reducing the death rate the results though suggestive are not statistically significant.

WOLMAN (p 933) reports on the whole favourably on the treatment of typhus with the serum of horses immunized by injections of increasing doses of living rickettsiae from the intestines of infected lice. The serum is administered subcutaneously and to be effective must be given early

URRA (p 1019) has had considerable success in the treatment of typhus by the method of Daniélopou in which intravenous injections of 250-500 cc.

of a solution containing 0.5 gm. chlorine and 8.5 gm. sodium chloride in 1 000 cc. of water were given once or twice daily. The fatality rate was reduced and although the duration of the fever was not affected, there was striking improvement in the neurological manifestations. These cases were treated in Spain.

It is usually thought that lice infected with typhus live only a few days but MACCHIAVELLO (p. 385) has found evidence that they may live for a month or more.

DAVIS and WHEELER (p. 743) report experiments on powders tested on man for their louse-killing properties. Details are given [but these powders have now been superseded by DDT]. DAVIS *et al.* (p. 744) succeeded in reducing almost to nil the louse population of the inhabitants of certain Mexican villages in which typhus was epidemic by the use of anti-lice powders and a preparation for the head.

DAVID (p. 664) points out the disadvantages of hydrogen cyanide as a fumigant for louse destruction, and mentions several substances on which work is being conducted and which may prove to be useful for this purpose.

Flea Typhus

PINTO (p. 27) has found typhus in the rats of Lisbon. A strain of pathogenic rickettsia was isolated from a pool of brain tissue from 5 *Rattus norvegicus*.

BERGZ *et al.* (p. 664) report cases of murine typhus in man in Tunisia. rickettsiae have also been isolated from the brains of rats in the same neighbourhood.

In the Ruanda Urundi district of the Belgian Congo NEUJEAN (p. 1014) noticed, in 1939 a steadily increasing number of sera which gave positive reactions to *Proteus* O\19 and O\2. Rickettsiae were isolated from lice collected from the patients and from rats and though the production of orchitis in guinea-pigs injected with these strains was by no means constant the author concludes that the epidemic was of murine origin. The disease was of low virulence and was widespread over a large area. JADOT (p. 1015) also has isolated strains of rickettsiae from rats at Coquilhatville in the Belgian Congo and has shown that the disease *fièvre rouge congolaise* is a form of murine typhus. In this the Weil Felix reaction with *Proteus* O\19 is not always positive nor are the rickettsiae always orchitic but they give cross immunity with strains isolated from cases of murine typhus. Lice can be infected *per rectum* with the rickettsiae and thereafter can transmit the infection, but the author states (without giving evidence in support of his opinion) that the vector is the rat flea.

In spite of the fact that it had been stated that fevers of the typhus group did not exist in Madagascar BAKER *et al.* (p. 29) report 16 cases in Diego Suarez, where the disease is apparently endemic. No animal experiments could be done so that no opinion on animal reservoir or vector is expressed, but the Weil Felix test was usually of the *Proteus* O\19 type.

J. C. PATEL (p. 118) reports a few cases of typhus in Bombay. the rat flea may have been the vector. In other cases lice and ticks have been suspected. V. D. PATEL (p. 387) also gives an account of several cases of endemic typhus in Bombay apparently of murine origin.

YU and YING (p. 25) give an account of 112 cases of typhus in Kunning. the disease was probably flea-borne and the attacks were mild.

PLOTZ *et al.* (p. 28) have found a considerable number of cases of endemic typhus in Jamaica under circumstances which suggest that transmission is effected by the ectoparasites of rats. The complement-fixation test to an endemic rickettsial antigen was positive in all cases.

CASTAÑEDA (p 1018) has found evidence which suggests that typhus of murine origin in Mexico may be spread from man to man by the human louse and considers that *R. prowazeki* and *R. mooseri* though different in some respects (notably in respect of cross immunity) are in other ways very similar that they may arise from a single strain and that strains intermediate between them can be found. The differences between them therefore are only quantitative. He advocates a combined vaccine made from animal lung preparations large doses of this injected 5-6 times at weekly intervals have proved satisfactory in laboratory workers.

MAZZOTTI and VARELA (p 28) have found infection of the murine type in a cat, in Mexico.

BECK *et al* (p 1020) have isolated a strain of rickettsiae from the brain of a wild rat in California.

BRICEÑO-IRAGORRY (p 28) notes that there are two forms of typhus in Venezuela—the murine and a type probably similar to Rocky Mountain spotted fever. He (p 391) has isolated rickettsiae from the brain of a rat (*R. norvegicus*) in Caracas Venezuela for the first time.

MACCHIAVELLO (p 385) has shown that murine typhus is transmitted from rat to rat by *Polyplax spinulosa* and *Xenopsylla cheopis*. He gives a list of bugs fleas mites and ticks in which transmission experiments were negative.

SORDELLI *et al* (p 388) have isolated strains of rickettsiae from cases of typhus in Argentina tests in guineapigs failed to show definitely whether they were of the murine type and in comment MEGAW suggests that rickettsia agglutination or complement fixation tests on the sera of the patients might achieve better results. The same authors (p 390) have isolated strains from *Xenopsylla cheopis* in the same area and have attempted to determine their type. The results however were highly irregular. The rickettsiae were of low virulence to the local guineapigs which apparently have a high degree of resistance. The report of another outbreak in man (p 390) again showed that the infection was mild and the results in animals inconclusive. The authors (p 391) have isolated strains of rickettsiae from rat lice and from bed bugs collected from the beds of two infected persons.

BEJARANO (p 388) notes that flea borne typhus occurs in Santa Fé Argentina.

MORAGUES and PINKERTON (pp 557-558) have found that mice inoculated with a given dose of murine typhus rickettsiae may develop either inapparent illness or fatal disease depending on the strain of mouse and the environmental temperature. An inbred strain was more susceptible than three ordinary strains and an external temperature about that of the human body led to a much lower mortality than temperatures 20-30 degrees (F) lower. It seems that the mortality rates can be approximately standardized by attention to these factors and that this may be useful if mice are used in assessment of therapeutic measures. The bearing of these results on typhus in man is discussed. MORAGUES *et al* (p 839) report that if penicillin is given to inbred mice infected with murine rickettsiae and if the injections are commenced soon after infection there is a favourable effect on the course of the disease. Secondary infection is eliminated but in animals which die the rickettsial infection is present. It seems reasonable therefore that penicillin may be useful in human disease if it is given early. GREIFF and PINKERTON (p 840) have found that penicillin injected into eggs in which murine rickettsiae are growing will inhibit that growth but will not necessarily destroy the organisms.

PETERSON (p 835) reports that in experimental typhus in mice the oral administration of Forbuzen is moderately successful and of toluidin blue very successful in preventing death but only if administration is started soon after infection.

Tests.

Weil-Felix reaction.—FELIX (p. 552) has summed up modern knowledge of the technique and interpretation of the Weil-Felix test. The details cannot be further abstracted, and should be sought in the original, but it should be noted that although a positive result at a titre of 1-100 or 1-200 is usually regarded as the limit in persons not suffering from typhus, in an endemic area the titre in the healthy may be considerably higher. The essential point is that in typhus the titre should show a pronounced rise in the course of tests made at intervals of 48 hours. High titre reactions are given in diseases of moderate severity—low titres are found in severe or very mild cases though in the latter they may be high. In comment, MEGAW gives the arguments in favour of a classification of the typhus fevers by arthropod vector rather than by the Weil-Felix test.

LEÓN and APODACA (p. 21) having tested the reaction to *Proteus* OX19 and OXK in healthy persons and in cases of typhus in Mexico conclude that titres of 1 in 320 or more are diagnostic with *Pr* OX19 and of 1 in 200 or more with *Pr* OXK. The antigenic structure of the rickettsiae contains 3 elements—the purely rickettsial element which always predominates, an element common to the rickettsia and *Pr* OX19 and one common to the rickettsia and *Pr* OXA which is the least important. The authors therefore see no justification for using the reaction to OXA as a basis for the classification of rickettsiae. In comment, MEGAW remarks that the diagnostic significance of these tests cannot be stated in terms of arithmetical figures and that positive reactions at 1 in 25 or 1 in 50 may be diagnostic in persons known previously to be negative. Low titres may be met in very mild or very severe cases.

GRATCH (p. 197) has found that in pregnant women not suffering from typhus, the Weil-Felix reaction with *Proteus* OX19 is positive in relatively high titre. He thinks, therefore that this may provide a simple early test for pregnancy.

Great fluctuations in the Weil-Felix reaction were observed by GAASE (p. 472) in a series of patients convalescent from typhus and tested every 5 days for several months. The effect of food is noted, and the author emphasizes the importance of making repeated tests in fasting patients. The same author (p. 378) reports that there is much variation in the titre of the Weil-Felix reaction in guinea-pigs given intracardiac injections of *Proteus* OX19 according to the diet of the animals.

ROBINSTEIN *et al.* (p. 659) have used injections of milk in an effort to provoke a positive Weil-Felix test in suspected cases with some success. On the other hand, BREYDO (p. 680) states that there is little value in this and similar methods.

Noting the variability of the *O* strains of *Proteus* X used for the Weil-Felix reaction, DE LA LASTRA SOURKIER (p. 470) states that by careful selection of typical *O* colonies it is possible to maintain suitable strains. He gives directions for the cultivation of these strains. BRIDGES (p. 534) has contributed a note, which should be read in the original, on the preparation of suspensions for the Weil-Felix test.

GAASE (p. 114) has investigated the thermostability of typhus agglutinins against *Proteus* OX19. The paper is very technical, and the original abstract should be consulted for details.

ZIRONI (p. 656) discusses the significance of the frequent occurrence of *Proteus* X19 in the blood of typhus patients during the early stages of the fever. The antigen common to *R. procyonae* and *Pr* X19 inhibits the antibodies which normally prevent *Proteus* from invading the blood stream, and thus allows

increased susceptibility to the latter. This antigen may serve as a source of vaccine against typhus [compare FELIX this *Bulletin* 1943 v 40 230].

Other tests.—STEUER (p 113) reviews the use of the dry blood agglutination test in a number of infectious diseases. In relation to typhus and with *Proteus* as the antigen this test is regarded by some workers as very useful in that positive reactions are given only with sera which give positive Weil Felix reactions in dilutions likely to be significant. BARDHAN *et al* (p 379) have used the dry blood test in Egypt, and conclude that subjects with typhus always give positive results but that the reactions may also be positive in conditions other than typhus. In some of their cases the dry blood test was positive when the Weil Felix was negative no explanation of this is given.

EYER and BRIE (p 23) describe a rapid agglutination test in which a dried suspension of *Pr OX19* stained with methylene blue on structureless paper is moistened with tap water and a drop of the blood to be tested is added. Agglutination is easily seen.

LEÓN and APODACA (p 379) have found a rapid slide test to be of some value in typhus though not so useful as the standard Weil Felix reaction.

VORONINA and MARKOVICH (p 1022) have devised a precipitation test in which the polysaccharide X fraction of *Proteus X19* described by CASTAÑEDA, is used to precipitate with serum. Preliminary work indicates that the test is useful and it is simpler than the Weil Felix.

An account of the technique of the complement fixation test in rickettsial diseases has been given by BENGTSON (p 738) but this must be read in the original. In working on complement fixation tests WERTMAN and PLOTZ (p 659) have found typhus antibodies in commercial dried and frozen complement the reason for this is probably that some of the guinea-pigs used for the preparation of complement may have been used in tests of typhus vaccine. Complement of unknown origin should therefore be tested for these antibodies. PLOTZ *et al* (p 1023) emphasize the help given in differential diagnosis of fevers of the typhus group by the use of the complement fixation reaction.

SMORODINTSEFF and FRADKINA (p 1021) describe a slide agglutination test, which depends on the fact that in the first few febrile days of typhus there is in the blood an antigen which can be detected by the complement fixation test but which disappears after the 6th-9th day when antibodies are formed. Details of the technique should be sought in the original abstract but the test is performed by mixing a suspension of carmine laden with antibody-containing serum with a suspension laden with serum from the patient. If the antigen is present agglutination occurs.

EYER and DILLENBERG (p 657) have compared the Weil Felix and the rickettsia agglutination tests in normal persons vaccinated subjects and patients with typhus. The results show that the rickettsia agglutination test does not give as many non-specific reactions in healthy persons and that it tends to become positive earlier in the disease than the Weil Felix. The authors claim that a persistently negative rickettsia agglutination test has never been observed in a proved case of typhus. In persons vaccinated and then hyper immunized by being bitten by infected lice during the preparation of Weigl's vaccine the titres of both reactions are surprisingly low.

KLIGLER and OLEJNIK (p 189) have performed the rickettsia agglutination test on patients with murine and with epidemic typhus. The results indicate that the test can effectively differentiate the two diseases. High specific agglutinin titres are found in rabbits after vaccination with murine and epidemic strains. In view of observed differences in antigenic pattern between different strains of the same type of rickettsiae the authors argue that vaccines should be polyvalent.

LUMMERZHEIM (p. 380) has used the intradermal test of Giroud in a series of cases of typhus. The test involves the skin reaction to injection of mouse lung vaccine and usually becomes positive about the 8th day remaining positive for at least one year.

Vaccination.

DIXON (p. 116) reports a series of controlled experiments in man in which the protective power of various kinds of typhus vaccine was assessed. The subjects were apparently infected 6-8 weeks after having been vaccinated. There was no evidence that vaccination had any influence in preventing attacks, but there was convincing evidence of the efficacy of killed vaccines of the Cox and other types in preventing death. Yolk-sac vaccines in which *R. prowazeki* and *R. mooseri* were mixed were not so effective as those made from *R. prowazeki* alone. [The author was a German storm-troop leader and the circumstances under which this experiment was made have been the subject of comment in the *Lancet*.]

As a result of observation of cases of laboratory infection with typhus in man TORRING (p. 740) states that if the disease occurs in persons previously vaccinated, the Weil-Felix reaction does not reach the high titres found in the unvaccinated, and that the diagnosis may easily be missed because the disease is mild and atypical. He thinks that vaccination may modify the disease so that it is not infective to lice and may thus break the man-lice-man cycle and therefore help to control epidemics. The strains in use in the laboratory concerned were both murine and classical, but in only 1 of 14 patients was the strain isolated. WOLFE and PATZER (p. 741) also make the point that after vaccination, persons who acquire laboratory infections do not seem to be infective to lice. Attacks in the vaccinated are usually mild, and the titre of the Weil-Felix reactions is low. The authors therefore think that vaccination may be an effective means of controlling epidemics.

A series of 4 laboratory infections with *R. prowazeki* is described by LARSEN and LENSE (p. 555) from Copenhagen. The method of infection was probably from droplets or inhalation of infected dust, or possibly from infective material on the hands. The workers were engaged with mouse lung preparations, three had been vaccinated, but one who suffered a severe attack, had not. TOKAREVICH and EPSTEIN (p. 1017) show once again, that typhus immunization by the Weigl method does not provide complete protection, but that the disease in the immunized is mild.

PENFOLD (p. 367) has recorded the *Proteus* agglutination titres of 23 healthy persons before and after vaccination with a Cox vaccine. Titres in general were low, and many of the subjects gave negative results. MEYER (p. 115) has found that after inoculation with the Weigl vaccine the Weil-Felix reaction is rarely positive at titres above 1-50, but that people so inoculated may, if they suffer from fevers other than typhus, show reactions up to 1-200.

MEYER (p. 473) shows that vaccination with the Weigl vaccine has no effect on the Citochol or Memcke reactions.

PARK and OFFENKANTZ (p. 471) have found that in persons vaccinated against typhus almost all were negative to *Proteus OX19* within one year. The response of many of these subjects, at some time to *Proteus OXK* in low titre is probably to be explained by the antigenic composition of the vaccine. In higher titre the *OXK* reaction still remains a valuable diagnostic test for scrub typhus.

OTTO and MAY (p. 663) make the point that the titre of agglutination of rickettsiae in vaccinated animals has no uniform relationship to the immunizing power of different vaccines, and that the relationship of Giroud's dermal reaction to the degree of immunity has still to be proved.

After a description of louse-borne typhus REGAMEY (p 200) notes that for the Swiss army the standard vaccine is a mouse-lung killed vaccine containing a mixture of *R. mooseri* and *R. prowazeki*.

Work on vaccines carried out in S Africa by BEVAN (p 835) shows that protection in animals against rickettsiae of tick borne typhus is much more effective with the homologous vaccine than protection against louse- and flea-borne rickettsiae with the homologous vaccines. Egg vaccines were found to be preferable to those prepared from animals especially in relation to tick borne strains. Repeated egg passage was shown greatly to exalt the virulence of all three forms of rickettsiae.

CLAVERO and PÉREZ GALLARDO (p 24) have maintained a strain of *Rickettsia prowazeki* by egg yolk transfers for almost two years during which time 92 passages were made. The strain typically virulent at first has become persistently non virulent for guinea-pigs and monkeys but has fully retained its immunizing power. If this strain remains non virulent but antigenic and if it is shown to be incapable of transmission from man to man by lice there is a possibility that it may be the source of an effective vaccine.

BARTH (p 657) has used a special strain of *Proteus* 119 for vaccinating against typhus. His results show that genuine immunity is conferred in three-quarters of the subjects subsequently tested by injection of blood from typhus patients and that the serum of vaccinated persons possesses power of neutralization.

Proteus OXA type Vector mite

A team of United States investigators reporting in the *Bulletin of the U.S. Army Medical Department* (p 841) describe what is known of the epidemiology and clinical course of scrub typhus. They note that penicillin even in maximum dosage has had no effect on the course of the disease.

Tsutsugamushi disease has been reported in troops operating in the Far East. AHLIN and LIPSHUTZ (p 745) report on the clinical features seen in 70 cases for details of which the original abstract should be consulted. The disease constitutes a serious military problem and prevention is of course important. Indigenous [and therefore probably immune] labourers should be used for clearing camp sites and the authors give advice on other means which may be taken to avoid infection.

MORISHITA (p 395) discusses the epidemiology of tsutsugamushi disease in Formosa and the Pescadores.

KRONTOVSKAYA (p 474) in the course of Russian research in rickettsial diseases states that a disease identified as Malayan typhus is seen in Central Siberia.

Intermediate type Vector tick

CAMERON (p 208) does not accept the generally held view that there is a marked difference in virulence between the eastern and the western strains of the rickettsia of Rocky Mountain fever. Studies on a large number of cases indicate that there is no significant difference in comparable age groups. The use of immune rabbit serum in the early stages of the disease seems to be of definite therapeutic value.

More cases of Rocky Mountain spotted fever have been reported from New York State by MAILLARD and HAZEN (p 474) and two cases are reported by RUBENSTEIN and ROWLEY (p 119) from Massachusetts.

READING and KLINT (pp 30 203) report 4 cases of spotted fever from Texas. From 2 of these rickettsiae were passaged in guinea-pigs and tests in animals indicated that the infection was of the Rocky Mountain type (ANIGSTEIN and BADER, p 206).

ANIGSTEIN and BADER (p 205) have inoculated suspensions of ticks (*R. sanguineus*, *A. americanum* and *A. maculatum*) collected in Texas into guinea-pigs. Several of the animals reacted with fever some with scrotal swelling. There is however no record of the isolation of rickettsiae.

BUSTAMANTE and VARELA (pp 394-844) have shown that the severe fever of the west coast of Mexico known by various names is immunologically indistinguishable from Rocky Mountain spotted fever.

GIBBONS (p 392) notes that 12 cases of Rocky Mountain fever have been reported in Canada. He gives an account of the distribution of various ticks and states that typical strains of virulent *R. rickettsii* have been recovered from Canadian *Dermacentor andersoni* from Alberta where fatal human cases have occurred.

SHELLEY (p. 203) reports 5 cases of tick typhus in Tanganyika Territory.

With the knowledge that bats may harbour the tick *Amblyomma cajennense* and on the supposition that they might therefore if susceptible, be reservoirs of the rickettsiae of tick-borne typhus MAGALHÃES and ROCHA (p 31) have investigated the susceptibility of various bats to the local strains. Two species of bats were found to be susceptible to one strain of rickettsiae, but two other strains were not able to infect them. The vampire bat was not susceptible.

MAGALHÃES (p 31) refers to the pronounced neurotropic properties of the rickettsiae of tick-borne typhus of the Brazilian type. MEGAW points out that this disease differs in no essential respect from Rocky Mountain fever.

Although rickettsiae of the Rocky Mountain fever type were found to persist for long periods in the tissues of *Ornithodoros rufus* DAVIS (p 32) failed to achieve success in a large number of attempts to transmit the infection by the bite of these ticks. The same author however (p 32) has proved that *O. parkeri* can transmit the infection by bite and that the progeny of infected ticks can also transmit by feeding. Transmission was effected by larvae, nymphs and adults and one female was infective 904 days after the infective feed. Offspring to the 4th generation were infective, 1,333 days after the infective feed, in one instance and fasting for one year did not prevent infectivity. The rickettsiae maintained full virulence. DAVIS (p. 303) notes that *Ornithodoros nicollii* is able to transmit Rocky Mountain and other similar fevers under laboratory conditions—transmission through the egg occurs.

PLÖTZ *et al.* (p 842) describe a complement fixation test by which Rocky Mountain spotted fever can be differentiated from boutonneuse fever. The rickettsiae contain a common antigen, which is soluble in saline but they also contain insoluble antigens which are specific and which react (at significant titres) only with homologous sera. The presence of the common antigen however indicates the relationship existing between the two diseases.

TOPPING *et al.* (p 29) show that sera from three cases of sporadic typhus in India tested by the complement fixation technique of Bengtson, reacted more strongly to an antigen of the Rocky Mountain fever type than to antigens of the epidemic or endemic typhus types. In comment MEGAW urges that this and the rickettsia agglutination test should be used more widely in India to determine the forms of typhus seen there since other methods of differentiation have not been satisfactory.

ANIGSTEIN and BADER (p. 685) have shown that injection of rabbit serum immune to Rocky Mountain fever rickettsiae into guinea-pigs simultaneously with, and at the site of intradermal injection of infective suspensions of the rickettsiae will prevent reaction in the animals but will not prevent development of protection unless the dose of immune serum is relatively large. The same result is obtained if the serum is injected up to 48 hours after administration of the infective material, but not beyond.

Successful treatment of a series of patients with Rocky Mountain spotted fever is reported by BAKER (p 207) who used for each injection 0.3 gm. procaine penicillin dissolved in 10 cc. of an aqueous solution of 1:1000 Metaphen. Administration was repeated at intervals of 3 or 4 days.

A formal phenol preparation of infected ticks (the Spencer Parker vaccine) has been used with highly satisfactory results in Brazil where tick borne typhus is becoming an increasingly serious problem. PIZA (p 208) recommends that vaccination should be carried out twice during the first year and repeated once each year afterwards.

Q fever

A summary of the epidemiology of Australian Q fever is given by DERRICK (p 558) this can hardly be abstracted further.

PARKER and KOHL (p 277) have found *Rickettsia diaporica* in *Amblyomma americanum* from Eastern Texas.

Bullis fever

LIVESAY and POLLARD (p 209) report laboratory work on Bullis fever which leads them to conclude that it is caused by rickettsiae which may be transmitted by ticks or mites in the Camp Bullis area of Texas. In the first report of this fever (WOODLAND *et al.* p 34) the clinical description suggested rather a disease of the dengue group but the present authors have found small red-stained rods and coccoid bodies in the cytoplasm and nuclei of cells from the spleen and peritoneum of infected guinea pigs when these were stained by Macchia's method. There was no cross immunity with other rickettsial diseases.

ANIGSTEIN and BADER (p 395) have isolated a strain of rickettsia from *Amblyomma americanum*. Immunity tests suggest that this is the infective agent of Bullis fever. These authors (p 666) in a more complete investigation of Bullis fever have shown that the infective agent is present in the blood of patients and in *Amblyomma americanum* collected in the area. Infection of animals did not immunize them against Rocky Mountain fever or Q fever but did so against subsequent infection with patient's blood. The findings in guinea pigs closely resembled those caused by mite-borne typhus and rickettsia-like bodies were found. The authors therefore consider Bullis fever to be a tick-borne rickettsial disease but note that the symptoms in man may closely resemble dengue there is no reaction with *Proteus*.

Trench fever

BERNSDORF (p 119) gives a general account of trench fever as it was seen in the German army during the war with a classification of the clinical types. He argues that *prima facie* a rickettsia is not likely to cause a disease with a pronounced tendency to recurrence and states that no treatment has been found to have any effect. The disease always ends in recovery. REIMER (p 120) and SKUJA (p 121) also give detailed clinical descriptions of trench fever.

The neurological features of trench fever are dealt with by ERNST and PORTIUS (p 559). The range of diseases which can be simulated is apparently very wide.

ECKARDT (p 277) thinks that the neurological manifestations of trench fever are due to localized myelitis affecting the posterior horns of the spinal cord.

KUMMERLING (p 277) shows that there is yet no diagnostic test for trench fever and that no drug has been found to have any curative effect there is danger in the use of any habit forming drug in a prolonged disease of this kind. WINDORFER (p 561) however has found Omnadin very useful. HESSE and KREMSER (p 1024) write of the use of X rays in the treatment of trench fever.

Studies on Rickettsiae.

WEISS (p. 378) has studied *R. prowazeki* by electron microscopy. The pleomorphism of the organisms was clearly shown. BROG *et al.* (p. 838) describe certain inclusion bodies found in association with typhus rickettsiae in animals. They discuss their origin.

FIELDING (p. 24) describes a modified Breal method for staining rickettsiae, and VYKA (p. 835) a method for staining rickettsiae in histological sections.

Charles H. Ilcock

MALARIA

RODMAN J & VAN HOOFT M. T. Recherches sur l'anophélisme en Belgique (Deuxième communication). [The Anopheles of Belgium (Second Communication)] *Ann Soc Belge de Med Trop* 1943 Sept-Dec v 23 Nos. 3-4 209-18 2 maps.

LEVY, R. J. A. W. The Anopheline Mosquitoes of Melanetha. *Trans. Roy Soc. Trop Med & Hyg* 1945 July 39 No. 6 489-501 [13 refs.]

A note on *A. punctulatus* and its variety *modocensis*.

HIATT E. P. & QUINN Gertrude P. The Distribution of Quinine, Cinchonine and Cinchonidine in Fluids and Tissues of Dogs. *J. Pharm. & Exper. Therap* 1945 Feb v 83 No. 2, 101-5

The fate of administered quinine in the animal body has recently been receiving further attention. CHEN & GEILING [this *Bulletin* 1945 v 42, 348] have studied the mechanism of elimination of quinine and atabrin from the circulation and tissues. HIATT this *Bulletin* 1945 v 42, 178] determined the plasma levels of quinine, quinine, cinchonine and cinchonidine in man following single doses by mouth. The distribution of these four alkaloids in the tissues and fluids of 11 dogs has been studied by the present authors. Some of the animals were anaesthetized with sodium pentobarbital without obviously affecting the results. Solutions of the sulphates of these substances were given intravenously in equivalent doses at such a rate for 1½ hours that a constant level was maintained in the plasma for at least 30 minutes. Animals were killed at various intervals and determinations of the alkaloids made in tissues and fluids. The colorimetric method devised by BROWN *et al.* (not yet published by the authors) for the estimation of basic organic compounds was used. A description of the method is given in the present paper. It consists essentially in the extraction of the alkaloids with ethylene dichloride followed by reaction of this extract with methyl orange. After removal of excess of the latter the extract is acidified with HCl in absolute alcohol and read in a colorimeter. Comparison with a calibration curve made from data obtained in the same way indicates the amount of base present. In control experiments determinations indicated that the alkaloids were recovered in the proportion of 90-103 per cent of the amount added. [No doubt the latter figure represents the error of the method.] After equivalent doses of the four substances it was found that the plasma concentration and distribution in the tissues and fluids of dogs were approximately the same for each. The plasma levels in dogs showed much less variation than those previously obtained for man. The tissue/plasma ratio in cerebrospinal fluid, red cells, brain, bile and skeletal muscle was low but was high in the case of glandular tissues and lung. The ratios showed little

variation in spite of alterations in plasma levels thus indicating a rapid attainment of equilibrium between plasma and tissues. It is probable that the balance would be altered in different animals as the result of variations in the metabolic breakdown of the alkaloids
J D Fulton

BROWN J S. Soft Tissue Calcification Secondary to Therapeutic Quinine Injection. *Brit J Radiology* 1945 June v 18 No 210 183-4 5 figs

Calcified cysts in the gluteal regions discovered as an incidental finding during X-ray examination are considered by the author to have been caused by therapeutic quinine bihydrochloride (9 gm in 2 cc of water) injection. These cysts were seen in European or Indian patients only. African natives were curiously unaffected. They give no trouble but can often be detected by palpation.

The radiological characters of these calcified masses were sufficiently characteristic to enable the diagnosis to be made solely on the radiograph.

Diagnostic features are —

(a) They occur in the gluteal regions.

(b) They are oval in shape often with a tail of calcification along the needle track

(c) They have a mottled consistency

The author points out that this type of calcification may be seen in soldiers returning from the tropics. [They should not be confused with other types of calcification due to the worm infestation.]
Eric Samuel

LANCET 1945 June 2 687-9 Indirect Determination of Plasma Mepacrine in Subjects on a Suppressive Regime. Method suitable for a Field Laboratory [Army Malaria Research Unit Oxford (MAGRAITH B G et al)]

As recorded in an earlier communication [this *Bulletin* 1945 v 42 251] it has been found that under certain conditions which are discussed below

$$PM = K \times \frac{UM}{UNH_3}$$

where PM is the plasma mepacrine concentration in microgm per litre. UM is the urinary mepacrine concentration in mgm. per litre. UNH_3 is the urinary ammonia nitrogen in mgm. per 100 cc and K is a constant. The urinary mepacrine concentration can be measured by the method of KING and GILCHRIST [below]. The urinary ammonia may be measured either by the formol titration method (COLE 1933) or is a method depending on permutite base-exchange followed by nesslerization (FOLIN and BELL 1917). Permutite is added to neutral or weakly acid urine and it takes up ammonia. The supernatant fluid is removed, the permutite is made alkaline and the ammonia is again liberated into solution and can be estimated colorimetrically by adding Nessler's reagent. The figure given for ammonia by the formol titration method is 20 per cent higher than that by the other method.

Ten subjects were used for the tests and four observations were made on each. They had been on a suppressive régime of 0.1 gm. mepacrine daily for at least six weeks. They were given 500 cc. of water and samples of urine were collected at intervals of an hour. The mean value for the constant K in the above equation was 500 when ammonia was measured by formol titration and 420 when it was measured by base exchange. It is recommended that the measurements on the urine should be done in duplicate and that the mean value should be used for the calculation.

When direct estimations were made of the plasma mepacrine the standard deviation of the mean of triplicate estimations was ± 4.1 microgm. per litre.

the values of the mean ranged from 10 to 38 microgm. When the plasma mepacrine was calculated from the observations on the urine the standard deviation of the mean error (i.e. error of urinary field analysis plus errors inherent in the biological relation expressed in the equation) was ± 4.0 microgm. per litre if the formol titration method was used, and ± 5.6 microgm. per litre if the base-exchange method was used. The mean error is measured by the difference between the value obtained by direct examination of the plasma and that obtained by calculation from the urine. In view of the simple methods employed, the errors of the indirect method are remarkably small. This equation however is correct only for men who have been on suppressive mepacrine for at least six weeks. For other régimes of mepacrine administration it is necessary to calibrate the equation to suit that particular régime by making a series of direct measurements of plasma mepacrine and comparing them with the concentrations of mepacrine and ammonia in the urine (see BROWN and RENNIE below).
F Hawking

ANN TROP MED & PARASIT 1945 May 31 v 39 No 1 53-60 1 fig Factors affecting the Excretion of Mepacrine in the Urine. [Army Malaria Research Unit Oxford (MAGRAITH B G *et al*)]

The first part of this paper describes in greater detail the observations which led to the conclusion that the relation between plasma mepacrine, urine mepacrine and urine ammonia could be expressed by the above equation

$$PM = K \times \frac{UM}{UNH_3}$$

Nine volunteers who had been on suppressive mepacrine (0.1 gm. daily) for some weeks were given ammonium chloride or sodium bicarbonate to make the urine acid or alkaline respectively. It was found that although the dosage of mepacrine remained constant, the excretion of mepacrine was much greater (up to 10 times as great) when the urine was acid, than it was when the urine was alkaline. In general, the mepacrine output increases as the pH decreases. The relation between urine mepacrine output and titratable acidity was fairly close but not so close as that between the urinary output of mepacrine and the urinary ammonia.

Plasma mepacrine (microgm per litre) = 151 urinary output of mepacrine (mgm. per hour) - 73 urinary output of ammonia (mgm. nitrogen per hour) + 20.3 but the equation $PM = K \times \frac{UM}{UNH_3}$ is easier to use since it involves the concentrations in the urine and not the volume of urine and it is practically as accurate.

Reference is made to the paper of BROWN and RENNIE [below] and it is emphasized that the above equation holds only for men who have been on suppressive mepacrine for some weeks. At an E.M.S. hospital six patients were studied who had received a therapeutic course of mepacrine. The concentration of mepacrine in the plasma was calculated from estimations of urinary mepacrine and ammonia by means of the first equation given by BROWN and RENNIE. The results were in fair agreement with those obtained by direct examination of the plasma. In 3 patients the agreement was very close. In 2 patients the indirect estimate was 40-48 per cent. too high.
F Hawking

BROWN M. & RENNIE J. L. Indirect Determination of Plasma Mepacrine during a Therapeutic Course. *Lancet* 1945 June 2, 686-7 2 figs.

Observations were made on the relation between plasma mepacrine on the one hand, and urine mepacrine and urine ammonia on the other. These

observations were made in 35 patients who had received a therapeutic course of mepacrine 0.2 gm. four times daily for 2 days and then 0.1 gm. thrice daily for 4-10 days. The specimens of plasma and of urine were collected 12-15 hours after the last tablet had been administered. The urine ammonia (UNH_3) was measured by formol titration in mgm per 100 ml. The plasma levels of mepacrine (PM) ranged from 14 to 75 microgm per litre and the urinary mepacrine (UM) concentrations ranged from 1.3 to 19.3 mgm. per litre. Under these conditions

$$\text{PM} = \frac{\text{UM}}{\text{UNH}_3} \times 109 + 27$$

or a better fit for the data was given by the equation

$$\text{PM} = 2.36 \text{ UM} - 0.42 \text{ UNH}_3 + 47$$

Further observations were made on 51 patients admitted to hospital with malaria who had taken suppressive mepacrine irregularly for as long as five months. The plasma mepacrine concentrations ranged from 0 to 35 microgram per litre and the urinary mepacrine concentrations ranged from 0.03 to 2.50 mgm. per litre. For these patients $\text{PM} = 7.3 \text{ UM} - 4$.

Another series of observations was made on 36 patients who had finished the above therapeutic course of mepacrine. The plasma mepacrine concentrations ranged from 12 to 100 microgram per litre and the urinary concentrations of mepacrine from 0.9 to 17.0 mgm per litre. For these subjects $\text{PM} = 1.5 \text{ UM} + 28$. Clearly the dosage of mepacrine used has a strong influence on the relation between the concentration of mepacrine in the plasma and that in the urine. The authors emphasize that the laboratory manipulations for the indirect method of estimating plasma mepacrine by urinary examination are far simpler than those required for direct estimation by examination of the plasma. But they repeat that it is necessary to work out the relevant equation of prediction by parallel direct determinations on a sample of the group involved. [In view of the fact that four different equations have been given for four different groups of subjects this working out of the equation for each particular context certainly seems essential. The necessity for this preliminary investigation greatly diminishes the advantages claimed for the simplicity of this indirect method of measuring plasma mepacrine.] *F. Hawking*

KING E. J. & GILCHRIST Margaret. Field Method of estimating Mepacrine in Urine. *Lancet* 1945 June 2 686

The method makes use of a Lovibond All Purposes Comparator or Nessleriser fitted with special mepacrine discs ranging from 0.5-5 mgm. per litre (obtainable from Tintometer Ltd. Millford, Salisbury or from British Drug Houses Ltd.)

To 50 ml of urine in a separating funnel add 2 ml of 10 per cent. NaOH and about 100 ml of ether or paraffin. Shake well, allow to separate and drain off as much of the urine layer as possible. Wash by shaking with 10 ml of 10 per cent NaOH and draining off. (The shaking and separating can be done in medicine bottles by decanting and sucking off but a separating funnel is more convenient.) If the colour is to be read in the Comparator add 18 ml. N HCl. If it is to be read in the Nessleriser add 50 ml of N HCl. Shake well, allow to separate and drain off as completely as possible into the 4 cm. Comparator cells or the Nessleriser tubes. Compare with coloured disc. If globules of ether or paraffin remain suspended in the HCl extract and make the reading of the colour difficult the extract should be passed through a filter paper.

If the colour is too strong dilute 1:1 with N HCl and read again.

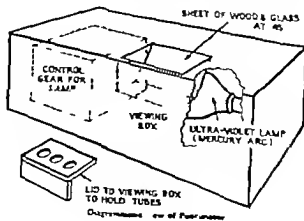
If the colour is too weak (i.e. less than 0.5 mg mepacrine per litre) 100 ml. (or 200 ml.) of urine should be extracted with the 100 ml. of ether or paraffin.

in a 500 ml. separating funnel. The mixture should not be shaken violently lest an emulsion form—it is sufficient to mix well by gentle inversion (about 1 a second) 30 or 40 times. The rest of the procedure is the same as above and the result is divided by 2 (or 4) F. Hawking

KING E. J. & GILCHRIST Margaret. Field Method for Direct Estimation of Mepacrine in Plasma and Blood. *Lancet*. 1945 June 30 814 1 fig

In a separating funnel are placed 10 ml. of 0.3N NaOH 25 ml. of petroleum ether and 25 ml. of the isopropylisobutyl alcohol mixture (redistilled isopropyl and redistilled isobutyl alcohol, equal parts) 5 ml. plasma (potassium-oxalate or citrate, or heparin) or 5 ml. whole blood is added and the mixture shaken vigorously for 1 min. and then allowed to separate. The blood layer is discarded. The mixture is washed with 10 ml. of 0.3N NaOH by shaking vigorously for 1 min. and the NaOH discarded. The NaOH wash is repeated twice and the NaOH layer separated as completely as possible. The mepacrine is next extracted into 5 ml. of the acid alcohol mixture by shaking vigorously for 1 min. After it has separated out, the acid layer is run off into a centrifuge tube and spun clear. 4 ml. of the clear solution is pipetted into a non-fluorescent test-tube. Alkaline borate buffer (1 ml.) is added and the green fluorescence compared with standard solutions freshly prepared by dilution with acid alcohol from the stock standard and treated with alkaline borate buffer in the same manner as the unknown. The fluorimeter requires about 10 min. to warm up and should be used in the dark.

The standard mepacrine solution contains 100 mg. per litre. [It is made by dissolving one 0.1 gm. tablet of mepacrine in one litre 0.1N HCl. It should be prepared monthly and kept in the dark.] A dilute standard solution is prepared by diluting 10 ml. of the strong standard to 1 litre with 0.1N HCl. This solution should be prepared freshly for use. Fluorescent standards are prepared as follows: 0.1 ml., 0.2 ml., 0.4 ml., 0.8 ml. and 1.2 ml. dilute standard are each diluted to 5 ml. with the acid alcohol mixture. 4 ml. of each of these is treated with 1 ml. NaOH-borate buffer. These are equivalent to 20 µg., 40 µg., 80 µg., 120 µg. and 240 µg. per litre respectively. Additional standards of intermediate strengths may be prepared if it is desired to match the blood strengths more closely. For very high mepacrine concentrations 2 ml. of whole blood may be used instead of 5 ml. For very low plasma concentrations, 10 ml. should be used instead of 5 ml.



[Reproduced from the *Lancet*.]

The fluorimeter (see figure) is used on a 220-240 volt AC circuit. It should be turned on about 10 minutes before use. The blood fluorescent tube is placed between two standards for matching. The tubes may be viewed vertically by placing them in the holes of the rack provided, or they may be viewed horizontally by removing the rack and placing the tubes in the well. Once the lamp has been switched off it must not be used again until it has cooled down. It should, therefore, be kept on continuously until each set of matchings has been completed. Suitable lamps are the Osira 80 watt black glass lamp 230 volt with choke as GEC leaflet 05 7196 or Phillips's MBW-V 'Phlora' ultraviolet mercury lamp with lampholder and choke. The whole apparatus in a convenient assemblage and readily portable form may be obtained from the Tintometer Ltd. Milford Salisbury at an approximate cost of ten guineas.

F Hawking

HENRY A J & GRINDLEY D N The Adsorption-Fluorescence Estimation of Mepacrine and Stilbamidine. *Ann Trop Med & Parasit* 1945 May 31 v 39 No 1 1-7 [11 refs]

Various improvements are described in the method devised by the authors for estimating stilbamidine in urine [this *Bulletin* 1943 v 4) 122]. Briefly this method consists of dropping small volumes of the fluid under test on to filter paper drying and comparing the fluorescence under ultra violet light with that produced by known concentrations of the compound. In the new technique a graduated 1 cc pipette is drawn out to fine capillary point with a right-angle bend 1.5 cm. above the end of the capillary. The pipette is filled with fluid and clamped horizontally the capillary end being in light contact with a filter paper. Fluid is allowed to run out slowly on to the filter paper so that there is very little free liquid on the paper at any one time. Altogether 1 cc. of fluid may be used. The stilbamidine present is adsorbed on to the filter paper. A small amount of water (0.2 or 0.3 cc) is then run through the pipette on to the filter paper in the same way to wash out urinary pigments or quinine. The paper is then dried and the fluorescence measured by comparison with standard papers any time during the next half year. By this technique stilbamidine may be detected in concentrations down to 0.02 mgm. per 100 cc [lower concentrations can probably be detected if a powerful lamp condenser and Wood's glass filter are used]. Mepacrine can be measured in urine by the same technique the range being from 0.25 mgm. to 10 mgm per 100 cc. in the original urine the accuracy is not very high. The application of this method is illustrated by the measurements of the mepacrine excreted in the urine of a patient treated for malaria. [This method is very simple and convenient for the estimation of stilbamidine for the estimation of mepacrine the method of KING and GILCHRIST above is more accurate and more sensitive.]

F Hawking

BUTT H R, HALL J E, WATKINS C H. & CRAGG R W Atabrine Dihydrochloride (Quinaerine Hydrochloride) some Observations on its Toxicity and on its Use in the Treatment of Malaria with particular reference to its Effect on the Liver. *Gastroenterology* 1945 Mar v 4 No 3 205-12. [17 refs.]

Fifty young men were studied who had suffered from multiple relapses of malaria [presumably due to *P. vivax*]. They had not received mepacrine for at least 2 weeks before this study was made and all but one were free from demonstrable malaria parasites at the time when observed. They were given 4.5 gm. mepacrine in 10 days by mouth 0.8 gm. being given on the first day

Liver function tests were carried out at the end of the ten days. In 48 of the men, a bromsulphalein test was done. At the end of the ten days the test was normal in all but one (a man who had a 6-12 per cent retention of the dye). The prothrombin time, serum bilirubin, haemoglobin estimation, erythrocyte leucocyte and differential counts were all within normal limits and so were special smears for macrocytosis. No significant changes occurred in the van den Bergh reactions, many of which were positive before treatment began or in the urine. Staining of the skin was clinically demonstrable in 18 of the subjects. Mild gastro-intestinal or other symptoms, especially diarrhoea, occurred in 21 of the patients but their significance is doubtful. Since all these men had suffered from liver damage during their previous attacks of malaria and 13 had had clinical jaundice, it is noteworthy that no significant signs of liver damage due to mepacrine were discovered in them following this course of treatment. This conclusion agrees with the results obtained at the Royal Army Medical College and in other military research units during the present war.

F. Hawkins

BERRY, J. N. Two Cases showing Cerebral Symptoms after Treatment with Quinaquine for Malaria. *Ind. & Med. Gaz.* 1945 Apr. 80 No. 4: 214

HEGSTED, D. M., McKIBBIN, J. M. & STARR, F. J. The Effect of Atabrine on Thiamine Deficiency in the Young Rat. *J. Nutrition* 1945 May 10 v. 29 No. 5: 361-3. 1 fig.

In previous experiments this *Bulletin* 1944 v. 41: 649] the influence of modifications of certain diet on the toxicity of atabrine (mepacrine) for young rats was investigated and atabrine was shown to have a choline-like or "choline-sparing" action. Further experiments are recorded in the present paper.

The same diet was used except that thiamin was omitted; the diet was given to 36 young male rats and 18 of them received also atabrine hydrochloride with the food—40 mgm. per 100 gm. of ration. After 13 days the animals not receiving atabrine began to lose weight; they were then divided into six groups and fed thiamin supplements. The results are shown in the table—

Group	Atabrine mgm. %	Weight at end of depletion period, gm.	Thiamin µgm.	Gain in 30 days, gm.	Gain of atabrine groups compared to control, %
1	0	17.0	3	7.5	
2	40	18.5	3	23.8	318
3	0	18.5	6	36.0	
4	40	16.0	6	50.0	139
5	0	24.8	9	60.4	
6	40	19.2	9	54.4	90

The experiment was repeated with the food consumption equalized in the control and the atabrine groups with a similar result. It was again repeated with equalized food intake giving the basal ration only as the diet and was continued until the rats died. The life of the atabrine rats averaged 43 days that of the controls 25 days; the former showed severe polyneuritis, the latter not as they died before such symptoms developed.

It was concluded that atabrine has a thiamin-sparing action.

J. F. Cowson

McCoy C. R. Suppressive Treatment of Malaria in Military Forces. *J. National Malaria Soc.* Tallahassee, Fla. 1945 Mar v 4 No 1 9-12

Extensive war experience has amply demonstrated the value of atebrium [mepacrine] 0.1 gm daily for suppression of malaria. It is much more effective than quinine, is better tolerated and preferred by troops. Many thousands of troops have taken atebrium in these doses for periods longer than a year with no evidence of toxic effects. Symptoms suggestive of intolerance—nausea, vomiting, and occasionally abdominal cramps and diarrhoea which may appear after one or more of the first few doses—are never serious and soon disappear if the drug be continued. True intolerance has rarely been observed. The maximum plasma concentration of the drug on a given dosage is not attained until after four to six weeks. In *falciparum* malaria atebrium in the above dosage not only prevents clinical attacks but also, if it be continued for four weeks after the last exposure to infection, cures the disease. Atebrium will not, however, prevent relapses of *vivax* malaria after the medication ceases. It may be necessary to continue suppressive treatment after exposure to infection has ceased in order to maintain military effectiveness. No evidence has appeared that long continued administration of atebrium produces drug resistant strains of plasmodia. The effectiveness of atebrium suppression tends to conceal the rate at which malaria infection is being acquired and may thus lead to neglect of antimosquito measures; this must be guarded against. The use of atebrium has been a very great help to military forces but it must not be regarded as a solution to the malaria problem.

Norman White

SYMES C. B. & HADAWAY A. B. Report on the Initiation of certain Experiments on the Use of D.D.T. for the Control of Malaria in British Guiana. 81 mimeographed pp. 1945 July 17

The authors arrived in British Guiana in January 1945 and, in consultation with Dr GIGLIOLI and Dr BEVIER, chose two sugar plantations and one rice growing area for their experiments. In these places malaria is hyperendemic and filariasis is common. The most important vector of the former is *Anopheles darlingi*, which breeds in canals, drains and other surface waters and which is domestic in its habits. It breeds throughout the year. Rainfall is heavy during the whole year (94 inches in Georgetown) but there are wet seasons during these there is breeding of *A. aquasalis* and *A. albipennis* but they are not important vectors. *Culex fatigans* is very common.

In the various places in which the experiments were carried out, examinations for malaria were made on the children and information was collected on the mosquito population.

The labourers on the sugar plantations live in quarters (known as ranges) which consist of blocks of 10 rooms with a verandah (gallery) along one side of the block. DDT was applied to certain rooms in the test ranges after a study of the mosquito population had been made and the results were compared with those of control rooms in unsprayed ranges.

The solution used was 4.6 per cent DDT in kerosene and the calculated dosage actually applied to walls, roofs, etc. was 2.05 quarts per 1,000 square feet—approximately 106 mgm. crude DDT per square foot. The results of one application were judged by captures of adult mosquitoes made in the rooms during several weeks. In one area (Lusignan) the reduction in captures of all species amounted to 95.9 per cent. of the control captures as late as the 7th week after the application. Evidence accumulated throughout the investigation that the effect of DDT is much greater on *A. darlingi* than on *C. fatigans*.

In the second area the verandahs of the ranges were treated in addition to the rooms; the results were again very satisfactory for several weeks. In the

third area, where rice cultivation was carried out and where the people lived in small houses of wood, mud and thatch or with iron roofs, DDT was used as a 5 per cent. solution in hydrocarbon oil and kerosene, as a 2½ per cent. solution, or as a 5 per cent. emulsion. Again the results were good as regards *A. darlingi* but not so good with *C. fatigans*. The weaker solution seems to be roughly as effective as the 5 per cent. solution and emulsion over a four week period. It remains to be seen from later observations how its toxicity will last. Mud walls, thatched roofs and painted or whitewashed wood seem to have reduced the efficiency against *C. fatigans* the reason is not clear.

At Lodge village 67 gallons of a 7 per cent. emulsion were discharged into the open air as a fine mist from a Hochberg Lamer generator. The facilities for mosquito breeding were abundant and it was found that at least 3rd and 4th stage anopheline larvae were killed to a distance of about 2 000 feet from the generator and probably further. First and second stage larvae (probably new hatchings) were found 48 hours after treatment. High rates of kill of adult mosquitoes were obtained in houses fairly close to the generator but 4 000 feet away the kill was only 18 and 52.3 per cent. respectively in two areas. The method holds promise of success but research is needed in various directions.

There is much investigation still to be done and the authors make specific mention of many of the points which need elucidation, in particular of the need to study the behaviour of solutions and emulsions, in various vehicles on the different materials used in building. They make the point that hand catching is a poor method of estimating residual mosquito populations and that better results are obtained after the use of a pyrethrum spray.

An interesting observation is that *A. darlingi* frequents ground shaded by vegetation during the day time and that spraying of the vegetation would probably not be successful in dealing with it unless the ground also were sprayed. The authors discuss in detail the types of sprayers tried in their work and the solvents used.

Complete tables of results are given, in great detail the original report should be consulted by those who are engaged on similar work.

Charles Wilcocks

GILROY A. B. & CHWATT L. J. Mosquito-Control by Swamp Drainage in the Coastal Belt of Nigeria. *Ann. Trop. Med. & Parasit.* 1945 May 31 v 39 No 1 19-40 3 maps, 4 text figs & 7 figs on 4 pls.

A full description is given of the rationale technique and results of draining mangrove swamps in the vicinity of Lagos for the protection of Service personnel from malaria. There is a difference of about two feet between the normal and the maximum high tides and in consequence there are three main coastal zones of vegetation with different characteristics: a low lying swampy fore shore, fringed with a belt of *Rhizophora* mangrove 20 to 400 feet wide exposed to all tides and not affording mosquito breeding places; a more or less open sandy shore only reached by high tides where there may be swamps, covered with marsh grass and *Avicennia* mangrove, with many crab holes and shallow pools, which constitute the main breeding places of *Anopheles melas* and relatively high land above the reach of spring tides covered with a dense growth of low bush, providing occasional breeding places for *Anopheles gambiae* and other anophelines in casual rainwater pools. The object of swamp drainage is to provide an embankment on the seaward side of the second zone to prevent access of high tides and to drain the land above the embankment to a low level channel made it and thence through one-way tide gates to the sea. The important second zone is thus dried out and most anopheline breeding comes to an end.

The low level drain and the embankment are made simultaneously the soil from the one being used for the other about 50 to 60 feet inland from the shore Tide gates in a standard concrete framework of which detailed plans are given, are then inserted in the embankment the sill being about 3 feet below mean sea level after which such main contour and subsidiary drains as are necessary are constructed in the area enclosed The embankment must be made good from time to time to remedy the effects of subsidence and wave action, and the more vulnerable parts may be protected by a thin concrete facing Tide gates cost £200 each and the total cost of reclamation amounted to £18 6s per acre 1 700 acres having been reclaimed by a labour force which varied between 700 and 800 1 300 acres were reclaimed in one year

The reclaimed area dries out very rapidly though occasionally low parts may need filling from neighbouring higher ground. Mosquito breeding in the *Avicennia* and marsh grass swamps ceases within a few days of completion of work and drainage channels remain free of larvae owing to the presence of numerous larvivorous fish. The work was followed by a marked fall in anophelines in nearby catching stations and in the malaria rate though credit must be shared between this drainage and the removal of the local population of gametocyte carriers following which the sporozoite rate of *Anopheles gambiae* dropped from 4.8 to 1.3 per cent Experiments have been made in the use of the reclaimed land and reforestation with *Melaleuca* and *Casuarina* species has been found possible data being presented on the results with these and other tree species.

[The paper is a useful contribution to our knowledge of control of *A. madas* and should be studied in the original by anyone undertaking work of this nature]

G Macdonald

THOMPSON P. E. The Effects of Sulfonamide Diets upon Infections of *Plasmodium elongatum* in Canaries. *J Infect Dis* 1945 Jan-Feb v 78 No 1 15-19

Though in common with a number of malarial parasites of birds *P. elongatum* reproduces by exoerythrocytic as well as by erythrocytic schizogony it is peculiar in that the exoerythrocytic development occurs not in cells of the macrophage or endothelial type but in various blood and blood forming cells. As COGGESHALL, PORTER and LAIRD [this *Bulletin* 1945 v 42 699] have shown that sulphadiazine and sulphapyrazine are able to eradicate exoerythrocytic forms of *P. gallinaceum* it seemed to the authors advisable to test the action of sulphonamides on the different exoerythrocytic forms of *P. elongatum*. In the tests carried out in canaries the drugs were administered in the food a special mixture having been devised which was sufficiently attractive to the birds to ensure that a fairly regular daily dosage was consumed. It was found that when the concentration of the sulphadiazine in the food was 1.3 per cent blood levels ranging from 15.1 to 26.4 mgm. per cent. were obtained. With a food concentration of 0.65 per cent. of sulphapyrazine blood levels of 12.8 to 20.3 mgm. per cent. resulted. It was found that food containing 1.3 per cent. sulphadiazine had no influence in the exoerythrocytic stages. The result was the same when the food concentration of sulphadiazine was raised to 2 per cent. and when food with 0.65 per cent. sulphapyrazine was used instead. When treatment was commenced before inoculation of parasites both drugs had some suppressive action on the infection

C. M. Wenyon

BLACKWATER FEVER.

BULL. U.S. ARMY MED. DEPT. 1945 Feb., No. 83 29-30 Fluid Intake after Hemolytic Transfusion Reaction.

Patients with injury of the kidney tubules are not infrequently "harmed" rather than helped by persistent efforts to secure diuresis by maintenance of fluid intake in excess of fluid output. It has been shown that "the patient with anuria tends to develop a marked plethora with a circulating blood volume far above the values for normal. Secondly clinical and pathologic evidence indicate that pulmonary edema is an important cause of death.

Anuria after intravascular haemolysis is due mainly to injury to the epithelium of the renal tubules and obstruction of the lumen of the tubules by haematin crystals is of secondary importance.

The best time to give diuretics is immediately after the onset of haemolysis. Two measures are recommended: (1) intravenous administration of one litre of isotonic 2 per cent. solution of sodium sulphate within a few minutes after the diagnosis has been made (successive signs are a sense of heat in the skin, headache a sense of constriction in the chest rigor and fever); (2) "fluid administration in excess of output by as much as 3 000 cc. only during the first twenty-four hours and mainly during the first twelve hours. Thereafter fluids are given strictly in accordance with demands of fluid loss.

The danger of persistent administration of fluids in excess of output are apparent regardless of the cause of anuria or oliguria [oliguria].

J. F. Corson.

MARGRAITH, B. Traumatic Anuria. [Correspondence.] *Lancet* 1945 July 14 68.

Referring to PARAMORE's letter [this *Bulletin* 1945 v 42 452] as a timely warning against the danger of giving too much fluid intravenously in cases of anuria, the author quotes from an article in the *Bulletin of the U.S. Army Medical Department* [above] and suggests that the treatment recommended in that article should be used in Britain in anuria due to blackwater fever crush injury and allied conditions. He disagrees with PARAMORE's statement that "whether the first or second convoluted tubules are the more affected can be neglected; however it be resolution of this question helps neither in prophylaxis nor in treatment" but, on the contrary he thinks that investigation of the nature and site of the lesion may lead to knowledge of what the lesion is and how it is produced.

J. F. Corson

 TRYPANOSOMIASIS

LESTER, H. M. O. Further Progress in the Control of Sleeping Sickness in Nigeria. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1945 July v 38 No. 6 425-44 [10 refs.]

In this paper the author continues his account of sleeping sickness control work in Nigeria to which he referred in 1939 [this *Bulletin* 1940 v 37 7]. He introduces his statement by a description of the characteristics of the disease as it is seen in Nigeria. Three forms are distinguished, the mild form (which is the most common and in which death is often due to intercurrent disease after a long period of ill-health) the toxic form (which is much more rare and in which death may rapidly supervene) and the nervous form (with

the characteristic sleeping sickness syndrome) Human trypanosomiasis became widespread when as a result of suppression of tribal wars people left the walled villages with their intensive surrounding agriculture and scattered into closer contact with the flies. There is now a correlation between the areas of infection and the lines of communication.

At first an attempt was made at control by a voluntary system of treatment but experience soon showed this to be insufficient and compulsory surveys with mass treatment were therefore started. The system is not carried to the same lengths as in the Belgian Congo where the aim is to examine every person twice each year for all the common diseases. This entails a very large staff and at one time there were 180 medical officers, 280 *agents sanitaires* and subordinate staff engaged on the work, each person was provided with a passport on which details of medical examination were recorded. In Nigeria however social conditions and the mildness of the disease were taken into account and the scheme adopted was less detailed than this. It consisted of the provision of teams for initial surveys and mass treatment and of permanent treatment centres at which attendance is voluntary after the main treatment has been completed. From these centres small surveys can be carried out and there is reason to believe that any recrudescence of the disease would soon be detected from the records of attendances and treatment. If incidence is reduced to about 1 per cent of the population these centres are adequate for control provided that new outbreaks are quickly dealt with.

The standard treatment now consists of three 1-gramme doses of antypol followed by five 2-gramme doses of tryparsamide at intervals of five days but the author gives an emphatic warning that a preliminary dose of 0.2 gm antypol should be given because with a larger initial dose alarming collapse or death may occur about once in 2 000 cases. In relapses such as are treated at the permanent dispensaries the standard course of tryparsamide is 17 grammes or even more after the three injections of antypol. There is no evidence that tryparsamide resistant strains of trypanosomes have been produced as a result of mass treatment in Nigeria but such strains have been produced where treatment is haphazard under a voluntary system. There is however no evidence of the spread of resistant strains by tsetse under natural conditions.

In a table which summarizes the work done from 1931 to 1943 it is shown that the peak of infection was reached in 1935 when the rate was 20.5 per cent. in the populations surveyed and that this has been reduced to 1.3 per cent. in 1942 and 2.1 per cent. in 1943. The great mass treatment effort was exerting its effect in 1936-40. In all over three million people have been examined in new surveys and over 900,000 in re-surveys during the period.

The sleeping sickness dispensaries have developed to include general medical and health work and provision has been made for the staff to be trained on those lines so that the dispensaries should become rural health centres. By the end of 1943 there were 43 dispensaries with 9 others under construction. Dispensary attendants trained in sleeping sickness work were also posted to 29 of the ordinary native administration dispensaries.

Tin mining has been a source of trouble. The miners suffered severely because their work was alluvial mining along the beds of streams heavily infested with tsetse. To control this it has been made compulsory for all miners to be medically examined every six weeks. This has been effective and the treatment given has reduced the rates of infectivity not only in the miners themselves but also in the neighbouring villages. In the gold fields also the examination and treatment of miners has effected a dramatic reduction: the rate has fallen from 35 to 0.4 per cent. Lester discusses the possibility of prophylactic injection of antypol but argues against it because of the danger of collapse after the injection, a danger to which it would be unjust to expose healthy men.

The tsetse flies concerned with sleeping sickness in Nigeria are *Glossina palpalis*, *G. tachinoides* and *G. submorsitans*. Clearing work has been done in the last few years to drive back the fly from immediate contact with human habitations and watering places and to protect the fords and traffic routes. For the river-haunting flies the amount of clearing needed has been too small to cause serious deforestation, and the methods used developed largely from the work of VASN have been successful so that in two provinces about 240 000 people are now protected. The Nigerian policy with regard to game destruction is one of *laissez-faire* because to reduce game would be to drive *G. palpalis* and *G. tachinoides* to depend upon man and domestic stock, and to increase game would be to increase *G. submorsitans*.

Sleeping sickness settlements are not easily created in a country so closely inhabited as Nigeria, and fly free areas are rare in that well watered land. But where the infection rates are high the concentration of the population in cleared country is deemed justifiable as in the eastern part of the Zaria province, where the rate was as much as 50 per cent. After much detailed preliminary work, which has been described in this *Bulletin*, the great Anchan corridor was prepared, and at present includes 480 square miles of fly free country in which model compounds have been constructed and where special attention had been paid to hygiene and to agriculture and stock raising.

The result of these activities has been that sleeping sickness is now almost under control. The depopulation which was taking place when the disease was at its height has been reversed to an increase in population but the fact that 21 000 cases were treated in 1943 shows that constant vigilance is necessary. [The author and those who have been associated in this work must be congratulated in these results largely achieved in war time when staffs have been greatly reduced. Research has lately been suspended, but proposals have already been made for a Central Trypanosomiasis Research Institute to be established in Northern Nigeria, and to serve the whole of British West Africa.]

Charles Wilcocks.

NIGERIA. REPORT ON THE MEDICAL SERVICES FOR YEAR 1943. Appendix B pp 19-21. Sleeping Sickness Service.

In 1943 the number of cases of sleeping sickness treated was about 21,300 of which 19 000 were dealt with by the Sleeping Sickness Service (5,321 at mass surveys, 13 100 at dispensaries and 540 at the mums). 830 were treated at missions and 1,500 at general medical stations. There was no evidence of any general increase of the disease though the total cases treated were greater than in the previous year partly because more permanent dispensaries had been established. Surveys and spot re-surveys were carried out and incidence rates of 3.8, 2.8, 1.0, 1.3, 0.2, 0.5 and 2.1 per cent were found.

Permanent treatment centres are established where surveys have been completed. There are now 43 of these and 29 Native administration dispensaries. At these in addition to the 13 100 cases of sleeping sickness 75,000 general cases were dealt with. In the mining areas the whole labour force of 6 000 was examined every six weeks and it was found that an average of 1.4 per cent. of the labourers contracted sleeping sickness every six weeks. But for these examinations and treatments rates of 20-40 per cent. would have again been general on these mines where the work is alluvial with intense exposure to tsetse.

Work on the Anchan settlement is continued. The system of partial clearing and barrier clearing used in much of the corridor is completely effective. Improvements in agriculture and stock farming are being continued.

In a conference with representatives from French and Belgian territories arrangements for closer co-ordination were made and a proposal was framed for the establishment of a Central Trypanosomiasis Research Institute

Charles Wilcocks

RODHAIN J & VAN HOOFT M T. Au sujet d'un élevage de *Glossina palpalis* en Europe et de quelques essais d'évolution chez cette glossine des *Trypanosoma lewini* et *cruxi*. [The Rearing of *G. palpalis* in Europe Attempts to infect it with *T. lewini* and *T. cruxi*] *Ann Soc. Belge de Méd Trop* 1944 June 30 v 24 Nos 1-2, 54-7

VAN GOLDSSENHOVEN C & SCHOENHAERS F. Sur la stabilisation des antigènes utilisés au sérodiagnostic des trypanosomiasés. [The Stabilization of Antigens used in the Diagnosis of Trypanosomiasis.] *Ann Soc. Belge de Méd Trop* 1944 Sept 30 v 24 No 3 167-73

Complement fixation tests were made with antigens prepared in various ways with *Trypanosoma equiperdum* obtained by fractional centrifugation of heavily infected blood. The chief defect was instability antigenic activity became progressively less with keeping and anticomplementary power became progressively greater. Various antigens tried e.g. ZOTTNER'S [this *Bulletin* 1934 v 31 593] MARKOWIECZ'S alcoholic antigen (*Deut Tierärztl Woch* 1941 v 49 578) and LUGOMER'S antigens (*Jugo-slav Vet Glasnik* 1940 v 20 300) were found unsatisfactory and the authors could not confirm WATSON'S view that frozen antigen would keep indefinitely.

A satisfactory antigen was finally prepared with the co-operation of RESELER (see *Ann Soc. Belge Méd Trop* 1944 v 24 29). The centrifuged deposit of trypanosomes was frozen, distributed into ampoules and dried in a vacuum at about -75°C. for an hour after which the ampoules were sealed *in vacuo*. This preparation was found to have preserved its antigenic power and a low anticomplementary activity for 16 months further tests may enable the time limit of preservation to be determined.

J F Corson

FIENNES R, N T W JONES E R & LAWS S G. The Course and Pathology of *Trypanosoma congolense* (Brodin) Disease of Cattle. 13 typed MS pp 22 figs. [59 refs.] 1945. Veterinary Research Laboratory Entebbe Uganda.

Native cattle adults and calves in Uganda were experimentally infected by subcutaneous injection of local virulent strains of *Trypanosoma congolense* and the resulting disease was studied by clinical observations, morphological and chemical examination of the blood and histological examination of the tissues.

The blood showed a great diminution in the number of erythrocytes and a corresponding decrease in haemoglobin the chemical determinations were almost always within the physiological range.

Although histological examination of the tissues supported the view that *T. congolense* is essentially a blood parasite with no invasion of the tissues severe pathological changes in the tissues were produced there was a widespread round-celled infiltration leading to fibrosis and necrosis. The organs most severely affected were the kidneys adrenals pancreas thyroid and pituitary. The authors regard these changes as primary and the anaemia as secondary. The fever was of a relapsing type in adult cattle the disease was usually fatal but calves usually recovered with immunity to homologous

strains but not to heterologous strains of the parasite. [No macroscopic examinations appear to have been made of the cerebrospinal fluid or of the pericardial pleural and peritoneal fluids] *J F Corson*

MAZZA, S. MIYARA S. & JORG M E. Investigaciones sobre enfermedad de Chagas. Exámenes histológicos de biopsias de conjuntivas en primer periodo de enfermedad de Chagas. [Histopathology of the Conjunctiva in the Early Stage of Chagas's Disease.] Universidad Buenos Aires. Misión de Estudios de Patología Regional Argentina (Jujuy). Publicación No 68. 1944. 80 pp. 76 figs. & 2 charts.

The authors have had the opportunity—and have taken full advantage of it—of examining sections of the conjunctiva taken by biopsy in the first stage of this disease.

They are careful to distinguish acute primary conjunctivitis from the secondary inflammatory reaction set up by extension from without. Only 4 per cent of cases presented the former. It is characterized by conjunctival erosion, much polymorphonuclear infiltration, distributed close to the epithelium with leishmania in numbers beneath the necrotic eroding zone. This leucocytic infiltration is very dense but does not invade the depth of the corium of the mucosa. Lymphatics are inflamed and appear as bands spreading to the submucosal vessels.

In the secondary inflammation the epithelium is affected, with eroded patches and hyperplastic and atrophic changes mingled. The subepithelial inflammatory tissue is composed in great part of plasmocytes with in some cases a moderate proportion of lymphocytes. In more than half the cases there is massive histiocytic proliferation, with giant cells in the interior of the infiltrated focus and leishmania in about one-fifth of the cases.

Eight cases of the primary form are presented, with much clinical detail: a history of the patient, a illness, the clinical state, the condition of the heart, the course of the disease and the treatment adopted.

As regards the eye lesions and their histopathology, with which the monograph is concerned, there is such a wealth of detail that we can give only a summary here: there is swelling and oedema of the corium with extensive congestion of the capillary vessels, dilatation of the lymphatics and small haemorrhages, infiltration in the deeper part of the corium, spreading gradually towards the epithelial layers and this may extend as a covering below the basal layer as a thin lining which the authors designate subepithelial permucous lymphangitis. The infiltration finally assumes the form of either a subepithelial stratum or a fusion into subepithelial nodules or granulations. Below the infiltration is oedema with sparse leucocytic invasion, while above the granulations (or nodules) or denser infiltration, erosion and ulceration take place with marked leucocytic invasion.

Photographs of the patients show the general condition, while a series of photomicrographs illustrate the histological changes. *H Harold Scott*

FEVERS OF THE TYPHUS GROUP

DOXOVICK R. & WYCKOFF R W G. Tests of Epidemic Typhus Vaccines. *Pub Health Rep* Wash. 1945 May 18 v 60 No 20 560-63.

This paper was approved for publication on September 11 1942 but because of the subject it has not been published till now.

The authors have produced evidence to show that great improvements had been made during the preceding year in the efficacy of the typhus vaccines and also that the titres of the complement fixation reaction in the sera of vaccinated guineapigs is a reliable indication of the potency of the vaccines. The results of the experiments on which these claims are based are shown in a table from which the reviewer has compiled the abbreviated table shown below. In the original table full details are given of the febrile reaction of each guineapig after a challenge intraperitoneal injection of brain substance of guineapigs infected by the Breinl strain of rickettsiae the table below contains instead a statement of the average number of days on which the animals showed a febrile response of 39.7°C or over these temperatures have been taken by the authors as indications of a significant febrile reaction. The number of days on which the temperatures were recorded was 10 starting from the 6th day after the administration of the challenge injection. The complement fixation tests were carried out three days after the second, and ten days after the first dose of vaccine had been given.

All the three types of vaccine were prepared from a common pool of inactivated yolk membrane vaccine I A was made by a development of the original Cox method vaccine II A was similar except that phenol was replaced by another chemical vaccine III A was processed on lines suggested by N. H. TOPPING

Vaccine dose (cc.)	Vaccine	Average febrile days after challenge	Average comp. fixn. titre	Number of guineapigs tested
0.1	I A	5.33	1-2	3
0.1	II A	2.00	1-16	3
0.1	III A	0	1-64	2
0.25	I A	3.5	1-32	2
0.25	II A	1.33	1-32	3
0.25	III A	0	1-128	2

In control unvaccinated guineapigs challenged in the same way the average number of febrile days was seven.

It is stated that vaccines made a year or more before the date of these experiments would probably not have given a demonstrable degree of protection or have been followed by a complement fixation titre in excess of 1-2 when administered in comparable conditions.

John W. D. Megaw

FITZPATRICK, Florence K. Vaccination of Mice against Typhus. *Proc Soc Exper Biol & Med* 1945 Mar v 58 No 3 188-90

Yolk-sac vaccines were injected intraperitoneally into mice which were tested for immunity 7 days later by intravenous or intraperitoneal injections of infected yolk sac material.

Of 54 mice immunized by various doses of epidemic typhus vaccine 53 survived 24 hours after receiving intravenous injections of epidemic typhus rickettsiae which killed 40 out of 64 unvaccinated mice within the same period. A dose of as little as 0.1 cc. of a 10 per cent. yolk-sac vaccine protected all but one of 8 mice.

All of 16 mice protected by the same epidemic vaccine survived 24 hours after being inoculated with a dose of murine rickettsiae which killed 3 of 16 unprotected mice in this case 8 of the 16 vaccinated mice died within 7 days.

as compared with 12 of the 16 control mice and it should be noted that the live murine rickettsiae were injected into the peritoneum not into the vein as in the previous series.

All of 8 mice protected by murine vaccine were found immune to intravenous injections of live murine rickettsiae whereas all of 8 control mice died within 24 hours when challenged in the same way. All of 8 mice similarly protected by murine vaccine were found immune to intraperitoneal injections of live murine rickettsiae while 5 of 8 controls died within 24 hours and the remaining 3 died after 7 days.

Of 8 mice protected by 0.5 cc. of a 10 per cent volk-sac suspension of killed murine vaccine 3 survived 24 hours after being challenged by doses of epidemic rickettsiae which killed all of 8 control mice in the same period.

The use of mice has two advantages: it eliminates the need for guinea-pigs and enables the period of testing to be shortened by about two weeks.

The results are said to suggest that the toxic factor in epidemic and murine strains of rickettsiae is identical.

John W. D. Meager

CLAYTON G. & PÉREZ GALLARDO F. Estudios sobre la cepa E de rickettsia *Proxazeki* viva en la inmunización humana. [Studies of Live "Strain E" of *Rickettsia proxazeki* in the Immunization of Human Beings.] *Rev. Sanidad e Hig. Pública* 1944 Nov. v. 18 No. 8 547-60.

The authors describe the results of further investigations into the "non-pathogenic and immunizing strain of *R. proxazeki*" whose discovery they announced in June 1943 [this *Bulletin* 1944 v. 41 24].

After preliminary tests with fresh living cultures the authors have now prepared a vaccine by desiccation in the manner employed in the preparation of yellow fever vaccine and have inoculated 2,217 persons in various parts of Spain where there was some risk of infection. Although no case of typhus fever has occurred among any of the vaccinated persons the authors do not claim that the efficacy of the vaccine has been established, but they have found that the Weil-Felix reaction becomes positive at titres of 1-40 to 1-640 in nearly half of the persons tested after inoculation. The strength of the reaction was not found to be affected by the dose of the live vaccine that was administered. Only one person had a reaction which might have been regarded as a mild attack of typhus fever: in this case there was continued fever from the 10th to the 21st day after inoculation.

The local and general reactions that occurred in a few cases were not more severe than those following T.A.B. inoculation.

John W. D. Meager

HOARE E. D. Some Additional Observations on the Presence of Agglutinins to *Proteus* O19 in the Serum of Pregnant Women. *Monthly Bull. Ministry of Health & Emergency Pub. Health Lab. Service* (directed by Med. Res. Council) 1945 June v. 4 125-8.

Like NELSON and CRICKSHANK [this *Bulletin* 1945 v. 42, 363] the author has been unable to confirm the claim made by GRATCH that the sera of pregnant women agglutinate *Proteus* O19 at high titres [this *Bulletin* 1944 v. 41 197]. Using suspensions issued by the Oxford Standards Laboratory he found that only one of 28 such sera reacted at a titre of 1-125. The readings were made after 3-hours incubation at 37°C. and 18 hours in the ice chest.

He then used a living culture of *Pr.* O19 selected from four strains as being the most sensitive and carried out slide-agglutination and the usual tube agglutination tests with the results shown in the table. In the slide test a portion of a colony was suspended in a drop of serum, either undiluted or diluted as shown in the table.—

	Slide Test					Tube Test				
	Positive at dilution of					Positive at dilution of				
	Sera tested	Undil.	1-2	1-4	1-8	Sera tested	1-25	1-50	1-125	1-250
Control	13	2	4	7	0	13	2	7	4	0
Pregnant	61	4	18	24	15	41	5	17	18	1

Although the average titre of agglutination was higher in the sera of pregnant than of non pregnant women the difference was not enough to form the basis of a test for pregnancy

SOHIER R. PARNET J. & CHON A. Recherches sur les réactions consécutives à l'injection intradermique de suspensions formolées de Rickettsies chez l'homme [Reactions following Intradermal Injection of Formolized Suspensions of Rickettsiae in Man] *Bull Soc Path Exot* 1944 v 37 Nos 1-2, 15-18

WU C. C. & CHI C. Y. Typhus Fever—a Clinical Study of 94 Cases. *Chinese Med J* (Chengtu Edition) 1944 Jan. v 62A No 2 67-70 Also in *Chinese Med J* Washington, 1944 July-Sept v 62 No 3 221-6.

Between October 1933 and November 1940 94 cases of typhus fever believed to be louse borne were seen by the authors at the Central Hospital, Kweiyang Hunan Province South China. The evidence pointed strongly to case-to-case infection. Among the 18 members of the staff who were attacked all but two had been in close contact with hospital patients no case of the disease occurred in July or August 1939 the peak periods being November or December. In some cases attempts were made to isolate rickettsiae but without success.

All the patients recovered, and it is stated that in 1937 HSIEN *et al* [this *Bulletin* 1938 v 35 362] reported 14 cases from Changsha and suggested that the mildness of the disease pointed to the occurrence of a strain of infection less virulent than that of North China. [It would not be surprising if the disease occurred in a mild form in South China where the climatic conditions are relatively unfavourable to louse transmission.]

The clinical features were of the type usual in mild forms of typhus fever the onset was sudden in 58 cases and gradual in 36 the usual duration of the fever was 12-16 days and the fall of the temperature was by lysis in 84 cases. The Weil-Felix reaction became positive before the end of the first week in four of the 68 cases in which the test was carried out in 22 it first became positive after the 14th day. The total leucocyte count was less than 5 000 per cmm. in 11 cases and more than 10 000 in 21. There was bronchitis in 17 cases and cough in 53. The maculopapular spots were scanty in 40 cases they became petechial in 41 in most of which the rash was profuse and the symptoms rather severe. No mention is made of the occurrence of septic or thrombotic complications.

John W. D. Megaw

LASEIN [Epidemiological and Diagnostic Value of the Investigation of Lice for Rickettsiae.] *Sovetskaya Meditsina* Moscow 1944 No 12, 15-17 [In Russian.]

Films were made from the gut of lice collected from supposed cases of typhus and were stained with Giemsa. In positive cases rickettsiae were found in large

numbers in the gut cells they could be easily distinguished from non-pathogenic forms which were larger and extracellular. Rickettsiae were present in gut smears of 8 of 15 lice collected from a case of typhus. 12 lice were collected from a second case and rickettsiae were found in nine. The test was also positive with lice from four members of the medical staff exposed to risk of infection. Three of these developed typhus after 9 to 13 days. In the fourth subject who remained well, lice were present in the outer clothing only. The test is useful in the early diagnosis of typhus since lice on the patient become infected in the first few days of the illness whereas the Weil-Felix reaction does not become positive until the seventh or eighth day. *D J Bauer*

HAMILTON H. L. PLOTZ H. & SMADEL J. E. Effect of p-Aminobenzoic Acid on the Growth of Typhus Rickettsiae in the Yolk Sac of the Infected Chick Embryo. *Proc Soc Exper Biol & Med* 1945 Mar v 58 No. 3 255-62, 5 figs

This report was presented to the U.S.A. Typhus Commission in December 1943 but was withheld from publication at that time.

Previous experiments by SNYDER, MAIER and ANDERSON (*Rep to Div Med Sci Nat Research Council*, Washington, 1942, Dec 28) and by ANDREWES, KING VAN DEN ELDE & WALKER [this *Bulletin* 1945 v 42, 20] had suggested that para-aminobenzoic acid ("PABA") inhibited the growth of rickettsiae in infected animals.

The authors describe tests of the action of the drug on the organisms growing in yolk sacs. The survival time of the chick embryos was prolonged and the number of rickettsiae in yolk-sac smears was greatly reduced by suitable doses of the drug injected into the yolk sacs on the day before inoculation with rickettsiae and a surprising degree of inhibition of the organisms was caused by injections given up to two days after inoculation of the yolk sacs.

The maximum inhibition was caused by relatively massive doses of 2-4 mgm. for each egg, but it was also found that large doses of 4 mgm. caused delayed death in a significant proportion of uninfected embryos.

The results were the same with both epidemic and murine rickettsiae.

John W D McGraw

BILIKIN. [Typhus in Vaccinated Subjects. *Sovetskaya Meditsina* Moscow 1944 No. 12, 14-15. (In Russian)]

Forty cases of typhus occurring in vaccinated persons were studied. 30 of these were experimental infections in volunteers. The febrile period was short (less than eight days in 30 per cent and less than 10 days in 50 per cent. of cases). The onset was rapid with rise of temperature without prodromal symptoms. marked fluctuations between morning and evening readings were common (1°C. in 20 cases, 2°C. in 14 cases). The exanthem was scanty and roseolar but was entirely absent from 13 cases. a typhoid state was seen in two cases only. Complications were rare (occasional bronchitis) and convalescence was rapid. The titre of the Weil-Felix reaction was never high (1/40-1/160) becoming positive at the end of the febrile period. Thus, together with the mild and atypical nature of the disease renders the diagnosis of typhus difficult in vaccinated subjects.

D J Bauer

VARGAS R. Aislamiento de una cepa de tifo murino en El Salvador (Isolation of a Strain of Murine Typhus in Salvador). *Bolet. Oficina Sanitaria Panamericana*, 1944 Nov v 23 No 11 680-83. English summary

In June 1943 a consistently orchutic strain of rickettsia was isolated from a patient on the 9th day of an attack of typhus fever. the patient's serum

reacted at a titre of 1-256 with the complement fixation test when a murine antigen was used with an epidemic antigen the reaction was negative. The test was carried out at the Army Medical Centre Washington.

The strain was maintained through 14 consecutive passages in guineapigs.

The fleas of more than 400 rats caught in San Salvador were tested by inoculation into 256 guineapigs with negative results but in a footnote the author states that in December 1943 rickettsiae were isolated from the fleas of rats caught in one quarter of San Salvador.

The clinical features of the disease in the patient were very similar to those seen in other typhus cases in Salvador.

John W D Megaw

MEGAW J W D Scrub Typhus as a War Disease. *Brit Med J* 1945
July 28 109-12

Seldom has a disease emerged from comparative obscurity to notoriety so rapidly as has scrub typhus. Its limitation to typhus islands in primary and secondary jungle inherent in its rickettsia mite-rodent cycle placed only sparse rural populations at risk until recently. It rarely obtruded in medical statistics and claimed the attention of only a few investigators in Malaysia and adjacent territories who were attracted largely by its kinship to the fevers of the typhus group. Since 1942 however the ebb-and flow of jungle warfare in those regions has vastly increased the populations at risk man in unprecedented numbers has in some degree supplanted the rodent as a host of the infected larval mite and the incidence of the disease has correspondingly soared. An average mortality of 10-15 per cent a high incapacitation rate and a depressing psychological effect has compelled intensive investigation by clinician entomologist and virus worker in South East Asia and in the South West Pacific. New minds and new methods have already greatly supplemented our previous knowledge of scrub typhus and devised effective counter measures. The incorporation of these (as far as security considerations permit) into this succinct report by so able a pioneer and so lucid an exponent in this field as Sir John Megaw is therefore most timely and valuable.

In discussing classification the author stresses the advantage of viewing scrub typhus in its true perspective as one of the four comprehensive groups of typhus-like fevers louse-borne flea borne tick borne and mite borne. To the clinician especially this is advantageous. Apart from the occasional occurrences of a necrotic ulcer at the site of the inoculation of the virus in scrub typhus and in the tick-borne *fièvre boutonneuse* the clinical syndromes including even such rare complications as parotitis and venous thrombosis are remarkably similar in all of the four groups. To the epidemiologist the association of the louse flea tick and mite in the nomenclature contrasts the genesis of the human or demic louse-borne typhus with that of the zootic members of the group. [It may be added that to the pathologist and the virus worker the similarities shared by the four groups are less fundamental. The human morbid anatomy and morbid histology are similar the causal organism is a *Rickettsia*. But the experimental pathology in its widest interpretation of mite-typhus is in so many aspects so different from that of the other three members of the typhus group of fevers that the virus worker of post war years will probably prefer to retain such individual names as *fièvre boutonneuse* Rocky Mountain spotted fever epidemic louse-borne typhus endemic flea borne typhus tsutsugamushi to mark differences that refinements of laboratory technique can demonstrate.

Referring to certain special features of scrub typhus the author notes that the disease is not new having as tsutsugamushi been known in Japan for ...

many years, and in China probably for centuries. The presence of the necrotic ulcer is not a *sine qua non* in the differential diagnosis. A disease of scrub-land in South-East Asia and the South West Pacific, it has literally dogged the footsteps of the Allied armies operating in those areas.

It is pleasing to see the name *R. tsutsugamushi* preferred to that of *R. orientalis* for the causal organism. For the organism was demonstrated in the tests of infected rabbits and the former name given to it by OGATA two years before NAGAYO *et al* working with the Chiba strain obtained from Ogata and with three strains from other sources re-demonstrated the organism in material from the eyes of rabbits, and in a report that received much greater publicity outside Japan than did Ogata's earlier report quite unjustifiably renamed the organism *R. orientalis*.

The salient known facts concerning the mite and its habitat are given and indicate clearly the many problems that confront the epidemiologist in attempting to cope with the disease by prediction and counter-measure. [The convenient term, blood meal of the mite should probably give way to the term tissue-meal or lymph-meal for it is now believed on secure histological observation that the larval mite after attaching obtains its nourishment by pre-digesting by salivary secretion the tissues of its host at the point of attachment to form a histosiphon.]

In its pathology scrub typhus is a disease of the smaller blood-vessels the vascular endothelial cells are invaded there is perivascular infiltration. Only exceptionally does convalescence fail to bring complete recovery from these lesions and their effects.

The clinical features are described in considerable detail and certain features are stressed which have puzzled many clinicians new to the disease, such as the undoubted occurrence of outbreaks of greatly differing degrees of virulence the inconstancy of leucopenia as a diagnostic point and the differing incidence of the ulcer in light and dark-skinned patients.

The West-Felix test yields positive agglutination of the OVA strain of *Proteus* and continues to be of great value provided that the strain of *Proteus* used is not maltreated and that interpretation is made with due regard to standards evolved by earlier serologists in this field. [Many observers would place the attainment of maximum titre in the fourth rather than in the second week after onset.]

Diagnosis affords little difficulty to the clinician experienced in the disease although unless the eschar be present he will usually desire to see the patient more than once in the first week before giving a confident diagnosis. Dengue, flea borne and tick borne typhus need to be excluded louse-borne typhus less so in the present combat areas. [Leptospirosis might well be added.]

In treatment, chemotherapy and serum-therapy have as yet failed. The minimum of transportation and the most expert nursing are two cardinal considerations. An adequate intake of fluid should be ensured. Supportive intravenous treatment should be undertaken only when expert laboratory help is available. [In this connexion recent observations made in Australia indicate the occurrence of marked diuresis a day or two before desquescence and by implication the possible promotion of pulmonary oedema by excessive intravenous fluids. Additional data on this point from different areas would be most valuable.]

Concerning prevention, methods of mite-avoidance, based on our knowledge of the mite and its host, are enumerated. But for security reasons mention of certain other effective methods of prophylaxis the result of recent investigations are withheld.

R. Leathem

J AMER. MED ASS. 1945 June 16 v 128 No 7 519 Protection against Scrub Typhus Mite.

The War Department recently announced that the Office of the Quartermaster General on recommendation of the Office of the Surgeon General is replacing dimethyl phthalate with benzyl benzoate for use in clothing impregnation for protection of troops against the scrub typhus mite so prevalent in the South Pacific. Clothing impregnated with benzyl benzoate will withstand more launderings before treatment is necessary than those impregnated with dimethyl phthalate. Clothing is dipped in an emulsion of 5 per cent. benzyl benzoate in water. One treatment is effective for about two weeks.

PATISO-CAMARGO L. DE ZULUETA, J & TORO G. Persistencia del virus de la fiebre petequial de Tobia en el Argasidio *Ornithodoros parkeri* [Persistence of the Virus of the Spotted Fever of Tobia in *Ornithodoros parkeri*] *Bol. Oficina Sanitaria Panamericana* 1944 Nov v 23 No 11 978-80 [10 refs.] English summary (5 lines)

An adult tick *O. parkeri* which had fed on October 29 1940 on a guineapig infected with the spotted fever of Tobia was titrated and injected into guinea pigs 1087 days afterwards. The infection was found to be almost as intense as that produced by the same rickettsial strain when the tick was originally infected. The strain was passed through 13 successive guineapigs. About three-fourths of the inoculated guineapigs died and there was a scrotal reaction in 47 per cent of the male guineapigs used in making the passages.

A related species of tick, *Ornithodoros rudis* is abundant in Tobia. It has been shown to be a potential vector of the local spotted fever and so may be important in maintaining and disseminating the disease.

John H. D. Megaw

BLAIR R. K. & BADER, M. N. Observations on Experimental Bullis Fever in Man. *Texas Reports on Biol. & Med.* 1945 v 3 No 1 105-11

Nine healthy young men were inoculated subcutaneously with spleen substance obtained from guineapigs infected with "rickettsia strains" regarded as the cause of Bullis fever.

Five of the volunteers received a strain of the 16th guineapig passage originally isolated from a tick *Amblyomma americanum* collected in the Fort Bullis area. The other four were inoculated with a strain isolated from a patient suffering from the disease. This strain was regarded as identical with the tick strain. [Many other attempts to isolate the causal organism from patients by cultural and animal inoculation methods had failed.] The febrile responses in the volunteers were as variable as those already observed by the authors in guineapigs. With the tick strain they were:—(1) fever (99-99.2°F) daily for four days; (2) no fever; (3) low-grade fever for 19 days; (4) low-grade fever for 18 days; and (5) low-grade fever for 24 days. With the human strain two of the patients had no fever, one had a daily rise to 99-99.4°F for five days and another had low-grade fever for 28 days.

In seven of the nine patients there was leucopenia with a relative lymphocytosis; the lowest total counts being 3700-4900 per cmm.

[See this *Bulletin* 1945 v 42, 639] for a previous reference to the specificity of the Bullis fever rickettsia.]

John H. D. Megaw

BRENNAN J. M. Field Investigations Pertinent to Bullis Fever. Preliminary Report on the Species of Ticks and Vertebrates occurring at Camp Bullis, Texas. *Texas Reports on Biol. & Med.* 1945 v 3 No 1 112-21

The author states that Bullis fever is the name given to an apparently new disease presumed to be rickettsial, endemic at Fort Bullis and strongly

suspected of being transmitted by a tick, *Amblyomma americanum* though a mite *Entomobula alfreddugesi* may possibly be concerned.

The area, of about 30,500 acres is semi-arid and uncultivated the vegetation consists of grass junipers oaks thorny shrubs and tangles of vines. Ticks of 12 species were found the most abundant was *A. americanum* which feeds on numerous hosts including man, and is known to be a vector of Rocky Mountain spotted fever. *Hemaphysalis leporis-palustris* was fairly abundant on rabbits in the area it transmits Rocky Mountain spotted fever and tularemia among animals but is not known to bite man. [STEINHAUS and PARKER (this Bulletin 1945 v 42, 373) have isolated a filter passing virus from two lots of this tick caught on rabbits in the Fort Bullis area.] The most abundant of the 22 mammals found in the area were the white-tailed deer (*Odocoileus virginianus*) the jack rabbit (*Lepus californicus merriami*) the armadillo (*Dasypus novemcinctus texanum*) and the grey fox (*Urocyon cinereoargenteus* subsp.) the racoon (*Procyon lotor fuscipes*) the fox squirrel (*Sciurus niger lincolni*) and the striped skunk (*Mephitis mephitis mesomelas*) were also common all the above harboured *A. americanum*. Small rodents were notably few in numbers and could not be important as hosts for the ticks.

Birds of 79 species were found the ground-inhabiting and bush-dwelling species were consistently infested by immature stages of *A. americanum* and so were regarded as important in maintaining the tick population.

Snakes of 16 and lizards of 8 species were found more than half of these were infested by the chigger mite, *E. alfreddugesi*. John W. D. McQueen

YELLOW FEVER.

LAGOS NIGERIA. Annual Report of the Yellow Fever Research Institute. 1944. 39 typed pp 1 fig (10 refs.)

As a result of discussions between the Secretary of State for the Colonies the Rockefeller Foundation and the West African governments it was decided that work on yellow fever should be reopened, and the Yellow Fever Research Institute practically closed since the departure of the Yellow Fever Commission in 1934 has therefore been re-established under Dr J. C. BUCHER and Dr R. G. HAIN of the Rockefeller Foundation. The Institute is situated at Yaba, Nigeria, and on its staff are an entomologist a medical officer and a laboratory superintendent, all from the Colonial Medical Service, a zoologist has also been appointed. The Institute is financed and controlled as a joint venture by the cooperating authorities the Rockefeller Foundation members arrived towards the end of 1943.

The programme for 1944-45 includes investigation into the distribution of yellow fever by means of a viscerotomy service protection test surveys and study of suspected cases work on these lines has been going on. It is presumed that jungle yellow fever exists, but this has not been proved it will therefore be necessary to test animal susceptibility to make protection test surveys in animals and to undertake studies on possible vectors of which only *Aedes aegypti* is at present known. Finally the question of the distribution and control of vaccine has received attention.

At Yaba a large mouse colony has been reorganized and the system of breeding used in Bogotá (Colombia) has been set up Details are given of this

and of the diet of the mice. The intracerebral protection test has been adopted as standard because it needs only 0.3 cc. serum and for other reasons. The determination of the amount of virus in vaccine is a standard procedure.

An ampoule is rehydrated in the amount of physiological saline solution customarily employed for vaccination. This is allowed to stand 20 minutes at room temperature and from this serial decimal dilutions are then made in 10 per cent. normal human serum in physiological saline. Twelve mice are inoculated intracerebrally from each dilution with each mouse receiving 0.03 cc. of the inoculum.

The mice are observed for three weeks and the deaths recorded. The end point of the titration is defined as that dilution of vaccine which will kill 50% of the mice under the conditions enumerated above. For example if the calculated endpoint is at a dilution of 1:1 000 then it may be said that the original material contains 1 000 fifty percent mortality doses or as has become customary 1 000 m.l.d. in each 0.03 cc. In the 1:10 dilution used for vaccination, there will be 100 m.l.d. per 0.03 cc. or 1 700 m.l.d. in each 0.5 cc. dose as actually administered.

The authors point out that with a dose of 100 m.l.d. in man there should only rarely be failure to immunize but to make sure that a sufficient dose is injected it has been considered advisable that not less than 1 000 m.l.d. shall be contained in each dose when the vaccine is shipped. These standards result in a minimum titre of 1:600 in vaccine distributed in West Africa. Batches with lower values are not approved for general distribution. Most batches have maintained their titre very well. During this period 13 blood specimens taken after vaccination have been tested for protection: all except one were positive.

In August 1944 an outbreak of jaundice was reported from places on the Cross River. The most severely affected district was Unwana, where there were more than 1 000 cases and 100 deaths. Yellow fever was suspected because the patients had fever, headache and albuminuria in addition to the jaundice. This outbreak was at once investigated but although a number of cases were fatal, all the evidence pointed to the disease being infective hepatitis. Yellow fever and leptospirosis were excluded. The authors think that the very poor nutritional state of the people was distinctly a factor in the severity of the disease. The investigations however indicated that there had been a severe outbreak of yellow fever between 1830 and 1835 as a result of which almost one half of the population was infected. The authors point out that yellow fever in Africans rarely follows the usual textbook descriptions.

The clinical concept of yellow fever must be a broad one and the physician should weigh the relative values of the presenting signs and symptoms. For example severe jaundice associated with a relatively mild complex otherwise is sufficient to exclude the diagnosis of yellow fever. Further albuminuria is the most constant finding in yellow fever and the failure to demonstrate it is a very strong argument against the diagnosis. In consequence it is concluded that the great majority of yellow fever cases in Nigeria are not recognized, especially in the African where the disease is so frequently mild.

In a pleasant and happy section of this report the story is told of the African Asibi from whom was isolated in 1927 the famous strain of yellow fever virus which bears his name and which was the origin of strain 17D so widely used as a vaccine. Asibi was seen by Dr MAHAFFY during his attack of yellow fever and has now again been found by Mahaffy: his serum is still strongly protective. Arrangements have been made by which Asibi will receive a pension for life.

The final section of the report deals with tests made on certain sera which had been left behind at Yaba since 1831-33. Many of these had originally contained protective antibodies, and full details of the tests made at the time were discovered with them. They had been left in an outbuilding exposed to all

the fluctuations of the surrounding temperature. In general there has been a marked reduction of protective power similar to that which occurs with diphtheria antitoxin under similar conditions. The average loss was of the order of 50 per cent. per annum, but there were great variations in individual samples.

Charles Wilcocks.

BRAZAVILLE [A. E. F.] RAPPORT SUR LE FONCTIONNEMENT TECHNIQUE DE L'INSTITUT PASTEUR EN 1943 [CECCALDI, J. Director]. 49-58. Fièvre jaune. Yellow Fever

Vaccination against yellow fever has been carried out during the year with three lots of vaccine (Nos. 133, 326 and 1074) received from the Rockefeller Foundation. A total of 719 persons were vaccinated including 563 Europeans, 64 local subjects, and 90 natives. Four showed more or less severe reactions on the sixth day which lasted for 48 to 72 hours. One lot of vaccine (No. 136) which had been kept for about 22 months in a Frigidarium at 8° to 10°C. when tested on mice was found to have lost its properties.

The "Dakar" neurotropic strain of yellow fever virus is recorded as being in its 456th passage in mice and regularly kills animals in a dilution of 1/600 000. The Saleum-Ceccaldi strain isolated at Dakar in 1937 is now in its 127th passage.

Serum protection tests were carried out in the village of Boundji (Lakouala Mossaka) on seven children: one was positive and six negative. At Brazzaville the sera of five men were negative but out of seven cattle two gave doubtful positives and out of ten dogs two were definitely positive.

Yellow fever was diagnosed in two Italian prisoners of war who died at Fort Archambault (Tchad) by pathological examination.

E. Hindle

LEANNETTE E. H. & PERLOWAGORA, Alma. The Complement Fixation Test in the Diagnosis of Yellow Fever. Comparative Value of the Serologic and Histopathologic Methods of Diagnosis. *Trans. J. Trop. Med.* 1945 Jan. v. 25 No. 1 11-19. [27 refs.]

The authors have studied the relation between the clinical severity of yellow fever infection and the amount of complement-fixing antigen in the blood, and find that there is a correlation between them. This is in marked contrast to the amount of damage found in the liver at death, which seems to bear very little relation to the severity of the infection.

The microscopical lesions occurring in the liver in yellow fever cases are well known but other conditions such as treatment with tannic acid may produce similar lesions (see BELT, J. Path. & Bact., 1839 v. 43 493). The authors inoculated 21 marmosets, *Callithrix jacchus* and 2 monkeys, *Macaca mulatta* with tannic acid. All these animals were examined for pathological changes in the liver and in 13 out of the 21 marmosets the histopathological features were indistinguishable from those considered characteristic of yellow fever. The changes included hyaline necrosis, fatty degeneration, and the development of typical intranuclear inclusions. The sera of these animals were examined for yellow fever virus and were uniformly negative.

A second table shows the results obtained in 10 marmosets and 4 rhesus monkeys which died as a result of infection with yellow fever virus. The histopathological diagnosis was negative for yellow fever in 4 out of the 10 marmosets and 2 out of the 4 monkeys. Nevertheless, yellow fever complement fixing antigen was present in the serum of every animal.

The results support the view that the complement fixation test constitutes a more accurate and reliable method of diagnosis of yellow fever infection than the histopathological examination of tissue such as liver.

E. Hindle

HARGETT M V & BURRUSS H W The Use of Rhesus Monkeys in the Testing of Aqueous-Base Yellow Fever Vaccine *Amer J Trop Med* 1945 Jan. v 25 No 1 19-30 1 fig [33 refs]

The present method of yellow fever vaccination involves the use of living virus attenuated to such a degree that it no longer produces visceral infection in men or monkeys yet the virus multiplies in the body and produces a high degree of immunity. The authors working in the Rocky Mountain Laboratory of the National Institute of Health U.S.A. have tested 192 different lots of aqueous-base (serum free) yellow fever vaccine in *rhesus* monkeys and give the results of their experiments in a series of tables and charts.

Each monkey *Macaca mulatta* was inoculated intracerebrally with 0.25 cc. of yellow fever vaccine from a single homogeneous lot. Each inoculum contained 200 to 2,230,000 minimum lethal mouse units [LD₅₀]. The animals were observed for a minimum of 30 days after inoculation and out of 200 monkeys none died of trauma or intercurrent disease.

Each monkey was bled on the 2nd, 3rd and 4th post inoculation days to determine if virus was present in the circulation. Evidence of its presence was found in 192 animals (96 per cent), more virus being present in those monkeys that had received a large dose of vaccine than in those receiving small doses.

Fever was shown by 167 monkeys in the majority of cases on the 8th to the 10th days and generally lasted for 2 days.

The sera of all the monkeys except one were examined both before and after vaccination by means of the mouse protection test. All the 199 animals were non-immune immediately prior to vaccination and all proved to be immune 12 to 33 days later. But of 102 animals receiving less than 200,000 m.l.d. of virus, 18 showed transient weakness with complete recovery and 4 signs of severe encephalitis with extreme weakness with or without paralysis. Of these four 2 were killed, 1 recovered and 1 had a residual paralysis of the right hind leg. Out of 98 animals receiving from 202,000 to 2,230,000 m.l.d. of virus 24 showed transient weakness with complete recovery and 8 developed severe encephalitis. One of these died and the other 7 were killed. Histopathological study of the brains of the 10 monkeys examined post mortem showed encephalitis in each case.

Twenty-two of the monkeys used had been previously infected with poliomyelitis, mumps, measles or Rocky Mountain spotted fever but no significant differences in their reactions were observed.

Of the 192 vaccines studied, 174 were released for human vaccination mostly in the United States Army. No icterogenic or other untoward reactions have been recorded and it is evident that serum free vaccine is preferable to that suspended in serum.

E Hindle

DENGUE

PITTALUGA G. Sobre un brote de Dengue en la Habana. [An Outbreak of Dengue in Havana.] *Rev Med Trop y Parasit* Habana. 1945 Jan.-Feb.-Mar.-Apr. v 11 Nos 1 & 2 1-3 1 chart.

In October and November 1944 there was a sharp outbreak of dengue in certain quarters of Havana. The disease was well known in Cuba in the early years of the present century but in recent times too little attention has been paid to it perhaps because of the absence of epidemics and the difficulty of diagnosis of sporadic cases.

The clinical description is very brief the fever is described as ending by crisis about the 4th day and no mention is made of the occurrence of secondary rises of temperature. [Both of the charts with which the paper is illustrated are of the monophasic type which often appears to predominate in places where the disease persists in endemic form. This monophasic type would be more likely to occur among patients who have a partial degree of immunity resulting from previous attacks.]

The rash appeared about the 5th day and lasted two or three days.

The author discusses the relationship of the disease to yellow fever and states that although the viruses of the two diseases have been shown to be different an experimental attack of dengue confers a partial degree of immunity on monkeys which are afterwards inoculated with the virus of yellow fever.

John W. D. Meyer

PAUL, W. D., ANTEN, E. H. & SAHS, A. L. A Dengue-like Fever occurring in Iowa during the Poliomyelitis Epidemic of 1943. *Arch Intern Med.* 1945 Mar., v 75 No. 3 184-91 1 chart [Numerous refs.]

The authors describe ten cases of a dengue like fever in which a thorough physical, bacteriological, and serological investigation failed to disclose any causal agent. All but one of the patients were perfectly well within eight days of the onset. The occurrence was sporadic there was no known contact between the patients, except that two brothers who had bathed in a creek about a fortnight before the onset were attacked on the same day. Three other patients had bathed in a lake creek or swimming pool, a short time before the onset. There was no evidence of transmission by an insect. All the cases occurred in the late summer six of them in August.

The fever was biphasic in three cases the second phase was shorter and less severe than the first. In five patients there was slight generalized lymphadenopathy and in one there was a fine maculo-papular rash on the extremities but this might have been caused by sulphathiazole. There was leucopenia in three cases the range of the leucocyte count was 3750-15000 per cmm.

Because of the general resemblance to dengue the authors prefer to call the disease a dengue-like fever they call attention to the general resemblance between their cases and the diseases described under the following names — (1) pretibial fever (2) dengue-like fever (CHENEY in North California, 1934-35 [this Bulletin 1936 v 33 446]) (3) Texas tick fever [Bull's fever] (4) New disease entity (Bowdoin in Georgia 1940) and (5) Colorado tick fever.

The incidence of the chief features of these diseases is shown in a table in the article. In Colorado tick fever and Bull's fever the infection is regarded as being tick borne in pretibial fever Bowdoin's fever and the present series of cases, there is a suggestion that the infection may be water borne.

John W. D. Meyer

LIPSCOMB, Laura L. & McMANIS, Jean L. Pretibial Fever. *J Amer Med Ass* 1945 May 12, v 128 No 2, 90-91 1 fig

A case is described which "clearly falls into the clinical category of pretibial fever" as described by DAXTERIS and GREYVAX [see this Bulletin 1944 v 41 278]. The fever lasted about nine days and was biphasic the first phase lasted six days, the second less than two days. A rash resembling erythema nodosum appeared on the 5th day, on the pretibial region, it faded somewhat at the end of the first phase but during the second phase it was more brilliant than ever.

The spinal fluid, examined on the 3rd day contained 52 mgm. protein, and gave positive reactions with the Lange colloidal gold test and the Wassermann test (using cholesterinized antigen).

John W. D. Meyer

PLAGUE

BROWN J H The Fleas (Siphonaptera) of Alberta, with a List of the known Vectors of Sylvatic Plague. *Ann Ent Soc Amer* Columbus Ohio 1944 v 37 No 2 207-13 [Summary taken from *Rev Applied Entom Ser B* 1945 June v 33 Pt. 6 88]

A list is given of the 53 species of fleas known to be present in Alberta, where sylvatic plague occurs showing their hosts and distribution there. Separate lists based on the records of Eskey & Haas are given of those among them that transmit plague and of the hosts on which these plague vectors have been found.

JELLISON W L Siphonaptera the Genus *Oropsylla* in North America. *J Parasitology* 1945 Apr v 31 No 2 83-97 3 pls. [19 refs.]

The American species of *Oropsylla* namely *O. alaskensis*, *O. arctomys*, *O. idahoensis* and *O. rupestris* have been reviewed. Present records indicate the following host relationships and geographical distribution.

O. alaskensis is restricted to the ground squirrels of the *Citellus parryi* group of the Far North, even entering the Arctic Circle.

O. arctomys is a characteristic parasite of the woodchuck *Marmota monax* but only very rarely occurs on other species of *Marmota* beyond the range of *M. monax*.

O. rupestris appears to be limited to *C. richardsoni richardsoni*.

"*O. idahoensis* shows less host specificity and is found on a great many species of *Citellus* and also on *Cynomys* in the Western States, Canada and Alaska. It is the most characteristic flea parasite of the squirrel subgenus *Callospermophilus* and its range roughly coincides with this host except in the Far North.

All species are found occasionally on rodents other than their normal hosts and frequently on predators within their range.

MUNTER, E J Pneumonic Plague. Report of a Case with Recovery. *J Amer Med Ass* 1945 May 26 v 128 No 4 281-3 3 figs. [Refs. in footnotes.]

Recovery from primary pneumonic plague is a noteworthy event and is very rare. The circumstances in the present case are somewhat unusual and their discussion turns on proof that the infection was primarily pulmonary, the treatment adopted and the precautions taken for preventing spread of infection to contact persons. The patient was a doctor, he had been engaged on plague investigation for 18 months and had had five injections of plague vaccine over a period of six months approximately one year previous to his illness. His illness began with malaise and chilliness, was accompanied by a hacking cough and quickly showed a temperature of 104°F with blood tinged sputum. One very important observation was that there were no buboes, nothing to suggest that this was pneumonia or septicaemic plague following local infection. Clinical evidence of pneumonia was an area of impaired resonance corresponding to an X-ray picture of a patch of infiltration. Plague bacilli were fully demonstrated in the sputum morphologically by culture and by animal injection. The author's approach to conclusion is cautious and may be quoted: "As far as I am aware this case is the first to be reported in which primary pneumonic plague has been treated by the use of sulfadiazine and the patient has recovered. However the recovery cannot be attributed solely to a favourable action of this drug since other factors may have contributed to it, as for example his previous immunization, the rapidity with which treatment

was commenced and the extremely careful nursing which he received. He was treated in an oxygen tent which also served to protect physician and nurses from infection. Some of the measures to prevent dissemination of infection were the wearing of masks hoods gowns and gloves by attendants which fortunately were entirely successful.

W F Harvey

DEVIGNAT R. Sur un phénomène de dissociation chromogène de la souche virus-vaccin F V de Girard et Robic Chromogenic Dissociation of the E.V. Strain.] *Rec Travaux Sci Méd Congo Belge* 1945 Jan No 3 120-27

Bibliographical references to dissociation of *Pasteurella pestis* are given under HADLEY [*Bulletin of Hygiene* 1927 v 2 437] POLLITZER with WE LIEB TEH *et al* [this *Bulletin* 1936 v 33 726] and other papers reviewed in *Tropical Diseases Bulletin* (1936-1940). The author while preparing the batch of vaccine E.V. 70 from the 104th passage found after 3 days at 26°C. that some of his Roux bottles gave in part an unusually heavy growth. This growth was examined microscopically and then subjected to control subculture test on glycerol-lactose agar and glucose agar. Isolated colonies of typical R and S types were obtained, both of which were of yellowish colour and both of which preserved their chromogenic characters. Further detailed tests were made of the morphological, cultural biochemical and biological characters of this new strain, which resulted in the conclusion that this phenomenon represented a chromogenic dissociation perhaps even a mutation giving colonies of typical R and S type. The strain is derived from *P. pestis* but its systematic classification is difficult whether in the genus *Flavobacterium* or along with the bacillus of *Malsaea* and *Vigani*. It is truly remarked that the precise systematic position of another organism allied to the plague bacillus—*P. pseudotuberculosis*—is not yet definitely settled.

W F Harvey

CHOLERA

JENNINGS R. K. Starch Digestion of *Vibrio cholerae* in Strongly Aerated Media. *J Bacteriology* 1945 Feb v 49 No 2, 163-6 [14 refs.]

Methods and media used in this series of studies have already been abstracted in some detail in this *Bulletin* [1945 v 42 377]. In this continuation study the statement that *V. cholerae* rapidly digests starch with production of acid but not gas, is investigated, and found to be true but not wholly true. Starch (1 per cent.) was substituted for the glucose in the continuously aerated salts C D-medium and its saccharification tested for at intervals, when—contrary to expectation—the pH " did not decrease at any time during growth. There was not at any time a significantly positive accumulation of glucose to give a reaction. The explanation offered is that the glucose if formed, must have been digested with considerable rapidity and the usual acid residue " also. A test of this explanation was instituted in which the glucose of the original medium " was replaced by (a) 1 per cent sodium formate (b) 1 per cent sodium acetate and (c) 1 per cent sodium lactate " with the result that no growth occurred in (a) but satisfactory growth developed in (b) and (c) especially in the (c) medium. The conclusion is reached that Heavy crops of *Vibrio cholerae* may be obtained in liquid media containing starch as the source of energy for reproduction without accumulation of acid by products provided that the culture is efficiently aerated. Good growth may also be

obtained when sodium lactate is used as the energy food. Neither of these substrates is so satisfactory as the previously described BRF medium for vaccine production.
W F Harvey

BERNARD P N & GALLUT J Recherches sur la toxine du vibron cholérique [Cholera Toxin.] *Ann Inst Pasteur* 1945 Mar-Apr v 71 No 3-4 65-82 [41 refs.]

PFEIFFER had originally contended that the toxin of the cholera vibrio was an intramicrobial endotoxin not a diffusible exotoxin and that it was set free only at the death of the organism. When METCHNIKOFF ROUX and SALIMBENI demonstrated by their collodion sac technique that rather suddenly after 2 to 3 days a fatal toxin diffused into the peritoneal cavity they considered that they had provided proof of the existence of a cholera exotoxin. It is this contention which is opposed by the authors. Important contributions to the discussion were made when LANDSTEINER and LEVINE [this *Bulletin* 1927 v 24 467] demonstrated the presence in the cholera vibrio of a complex (glucides fatty acid and phosphorus) capable of giving a polyside haptene and when BOIVIN MESROBEANU and MESROBEANU (*C R Soc Biol* 1933 v 113 490) isolated a complex and called it glucido-lipidic because it was a combination of a phospholipid and a polysaccharide. This complex represented the chief element of the endotoxin and the somatic O antigen. This is the historical background of the discussion which contends that the distinction between exotoxin and endotoxin is nowadays negligible and that there is one complex cholera toxin produced only at the death of the vibrio. It is capable of being split into a glucolipidic antigenic constituent which is of too high molecular structure to traverse the collodion sac and a non-antigenic protein like constituent which can pass the sac and which by its inability to give rise to any antitoxin is probably not an exotoxin in the true definition of that word. One of the authors, GALLUT has been a noted contributor [this *Bulletin* 1943 v 40 910] to knowledge of the constitution and action of the glucolipidic complex. The cholera toxin has been prepared from one of the best out of 200 Indo-China strains by growing it for 18 hours on glucose agar at pH 8 suspension in thrice-distilled water centrifugation to obtain a vibrio deposit resuspension in veal peptone bouillon incubation at 37°C. and final subjection to prolonged centrifugation to furnish the toxic supernatant fluid. This toxin, at least equal to the best that can be obtained from cultures after several days can be produced in 4 hours in glucose bouillon in which the organisms become autolysed by the acidification set up from their fermentation of the glucose. The glucolipid constituent of the toxin produces the congestion and visceral necrosis of cholera while the protein like but dialysable constituent determines the symptom of hypothermy.
W F Harvey

GALLUT J & GRABAR P Recherches immunochimiques sur le vibron cholérique. III Mise en évidence de deux constituants toxiques de nature différente dans la toxine cholérique [Demonstration of the Two Different Constituents of the Cholera Toxin.] *Ann Inst Pasteur* 1945 Mar-Apr v 71 No 3-4 83-92 [15 refs.]

Research into the nature of the cholera toxin has enabled the authors to define with precision the conditions favourable to rapid production of a very active toxin. The early work with intraperitoneal collodion sacs and dialysis was abandoned for fractionation by physico-chemical methods such as ultrafiltration through membranes of known and graduated porosity. It may be assumed that the molecules of the antigenic glucolipidic complex are very

voluminous, as the solutions are opalescent, and the authors' first effort was directed to finding the terminal point of filtration, that is to say the most porous membrane which retained the complex entirely and allowed the remainder of the total toxin to pass. This ultrafiltrate is a limpid yellowish liquid giving a strong iodine reaction and the chief reactions of proteins. True bacterial toxins are of protein nature but should also be antigenic which however the ultrafiltrate is not.

The glucolipidic complex is toxic in the dose of 0.05 mgm for a 15 gm. mouse of 0.5 mgm for a guinea-pig of 250 gm intraperitoneally and of 0.5 mgm. for a 2 kgm rabbit intravenously. The pathogenic features of the toxic ultrafiltrate are very characteristic and are represented by hypothermy.

A summary of the characters of the two constituents of cholera toxin gives them as I. *Glucolipidic endotoxin*—(1) 80–100 mu (2) neutralized by antiglucolipidic serum and by antiserum to total toxin (3) productive of congestion. II. *Toxic substance of the ultrafiltrate*—(1) 4 mu (2) not neutralized by antiglucolipidic serum or by anti-serum to total toxin (3) productive of hypothermy (4) probably protide in chemical composition possibly even protein. W. F. Harvey.

BACILLARY DYSENTERY

FORTUNE, C & FERRIS, A. A. *Diarrhoeal Diseases in New Guinea. Med. J Australia* 1945 Apr 7 v 1 No 14 337–44 [18 refs]

Among 2,849 patients with diarrhoea admitted to an Australian general hospital in New Guinea during a period of 18 months 36.0 per cent. were proved to have bacillary dysentery 1.4 per cent amoebic dysentery while the remainder were presumed on clinical and epidemiological grounds to have bacillary dysentery. [More careful bacteriological investigation in a smaller series reduced the proportion of cases in this last group.] Of 1,028 strains of dysentery bacilli isolated, 13.4 per cent were *Bact. shiga* 78.0 per cent. *Bact. flexneri* 8.0 per cent *Bact. ambigua* (Schmitz) 2.4 per cent. *Boyd type II* and 0.2 per cent. *Bact. sonnei*. A detailed analysis was made of the bacteriology, symptomatology and treatment of 503 consecutive cases of diarrhoea. In this group 54 per cent of 474 cases diagnosed as bacillary dysentery were confirmed bacteriologically by culture of both faecal specimens and rectal swabs (taken through the proctoscope see same authors *Bulletin of Hygiene* 1945 v 20 183) on desoxycholate-citrate agar. The majority of infections were classified as mild or moderate 18 per cent. of the Shiga infections and 6 per cent. of the Flexner cases were severe. Among 35 consecutive patients with Shiga dysentery sigmoidoscopic examination showed ulceration of the bowel in 20 and a strawberry-red oedematous mucosa in 13. The average stay in hospital for Shiga infections was 23.5 days and for Flexner infections 17.5 days.

Sulphaguanidine in large doses (initial dose 7 gm. followed by 3.5 gm. five times a day for 4 days and 3.5 gm. t.i.d. for 3 days) was given to all patients immediately after admission to hospital, and the results were uniformly good. Shiga infections responded better than Flexner infections. Only 30 cases (other than amoebic infections) had persistent or recurrent diarrhoea after a full course of treatment, and as these cases were bacteriologically negative and free of mucosal inflammation or ulceration they were classified as "irritable bowel." Patients were discharged when sigmoidoscopic examination was normal and one rectal swab was bacteriologically negative. On this basis 7 out of

179 (4.0 per cent) bacteriologically proved Flexner infections were carriers and on the 14th day after commencement of treatment 9 other Flexner carriers at this stage were found still to have pathological changes in the bowel.

Surveys for carriers were made in three groups (1) 120 healthy natives in a catering establishment where there had been no cases of diarrhoea for 3 months only one Flexner carrier was found (2) 50 men in a unit where Flexner infection was prevalent there were 5 Flexner excretors of whom 3 were convalescent carriers (3) 133 men in a unit affected with epidemic diarrhoea 7 carriers were found 2 of *Bact shigas* and 5 of *Bact flexneri* 4 of these were convalescent carriers Symptomless contact carriers responded well to sulphaguanidine convalescent carriers less well in 6 of 8 resistant cases in the latter category a course of sulphadiazine was effective. Some special points including treatment about amoebic dysentery are briefly discussed.

Robert Cruickshank

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

HAUER, A & DECKERT K. Erfahrungen mit der Kultivierung von Darmprotozoen als einem Nachweisverfahren [Diagnosis of Infections by Culture of Intestinal Protozoa.] *Deut Tropenmed Ztschr* 1944 Feb-Mar v 48 No 3-6 60-67 3 figs

Having found by experience that in many cases of intestinal protozoal infection a number of faecal examinations may have to be carried out on several days before such infections can be detected the authors investigated the possibility of simplifying diagnosis by the employment of culture methods. They came to the conclusion that the best results were obtained with the Dobell-Laidlaw medium consisting of a solidified serum base covered with Ringer-egg-albumin solution to which rice starch is added. It was found that in spite of buffering the pH rapidly fell from the optimum of 7.4. This was remedied by pouring off the liquid and renewing it each day. After three or four days owing to breaking up of the solid base it was necessary to subculture to fresh tubes. In this way it has often been possible to detect both amoebic and flagellate infections which could not be discovered by direct microscopical examinations of the faeces. The identification of the organisms in cultures is in many cases easier than in the faeces for a large number can be passed under review in a very short time. The differentiation of the culture forms requires some experience but to help the uninitiated the authors describe the chief characters of the various amoebae which may appear. It is of interest to note that they support the view that the small race of *E histolytica* is a separate species *E hartmanni* and that through a number of subcultures it shows no tendency to assume the form of the typical large *E histolytica*.

C M Weryon

SIMONETTI C. Sindromi epigastriche e tifo-appendicolari nelle coliti amebiche. [The Epigastric and Appendicular Syndromes in Amoebic Colitis.] *Boll Soc Ital di Med e Igiene Trop* (Sez. Entrea) 1944 v 4 No 4 685-96 English summary (7 lines)

Dyspeptic symptoms associated with gastro-duodenal disturbances are common in patients with amoebic colitis these vary in degree between the purely functional and the frankly organic some are a mingling of the two. Among 2400 whites (Italians?) examined on account of digestive

disorders at the Asmara Hospital in 3 years 4 months to August 1944 there were 355 (15 per cent.) with duodenal ulcer and 101 (4 per cent.) with gastric ulcer. 315 (13 per cent.) had amoebic colitis. Seventy-eight (all males) had amoebic colitis and duodenal ulcer and twenty-one (19 males 2 females) had the amoebic colitis with gastric ulcer. Among 200 natives attending the hospital for the same causes during the same period, 35 had a duodenal and 5 a gastric ulcer and 75 had amoebic colitis. Nine (all males) had duodenal ulcer and colitis—there were no cases of gastric ulcer and the amoebic colitis.

Next, appendicitis or an appendicular syndrome—pain in the right iliac fossa with colic—is common in amoebic caecitis and colitis. Of the 2,400 Europeans examined 318 (161 males, 157 females) had appendicitis. 45 males and 25 females had appendicitis and amoebic colitis. That is 28 per cent. of the males with chronic appendicitis had amoebic colitis also, and 16 per cent. of 157 females. As regards the indigenous population attending the hospital, 10 out of 67 males with amoebic colitis suffered also from appendicitis, and 3 out of 8 women. Further 10 of those with chronic appendicitis 26 in number were passing *Entamoeba histolytica* in their faeces. Of course in some cases of acute appendicitis the form was the usual type and might have no connexion at all with the amoebic colitis nor is it possible to say (in cases where operation was not performed) whether the chronic appendicitis was due to the *Entamoeba* or to the more usual causes. We can only say that chronic amoebiasis and chronic appendicitis may simulate each other and cannot always be differentiated (and may of course co-exist). The concomitant incidence of the gastric and duodenal ulceration and of appendicitis with amoebic colitis is so high that it is more than likely that the conditions may be aetiologicaly connected. This aspect of the question is to be dealt with in another paper. H. Harold Scott.

HERY R. S. Secondly Infected Liver Abscess treated with Penicillin. *Lancet*. 1945 Aug 4 133-41 6 figs.

LUIS CARRI E. Pseudo-epilepsia per giardiasis intestinal. Pseudo-Epilepsy due to Giardiasis. *Prensa Méd Argentina* 1945 Mar 18, v 32, No 20 903-6. [19 refs.]

RELAPSING FEVER AND OTHER SPIROCHAETOSIS

SCHWEITZ J. with the collaboration of H. BAUMANN & M. FORT. Sur quelques foyers cryptiques de *Spirochaeta duttoni* du Congo Oriental. [Some Cryptic Centres of *Spirochaeta duttoni* in the Eastern Congo.] *Ann Soc Belges de Méd Trop* 1943 Sept-Dec v 23 No. 3-4 219-36 1 map

During the course of a malaria expedition to the Eastern Congo in 1939 organized by the Royal Colonial Belgian Institute the author took the opportunity of trying to find *Ornithodoros* in the various localities visited between Lake Kivu and Lake Albert. *Ornithodoros montana* was found in five localities. Nyangazi at an altitude of 1 650 metres. Nzulu and Kisenyi on the banks of Lake Kivu at 1 460 metres and Bogoro and Gity two districts overlooking Lake Albert at 1 450 metres.

A total of 231 adults and 254 children from these five localities were examined for spirochaetes with uniformly negative results.

The ticks from Nyangazi were examined for spirochaetal infection by Professor ROCHAUD who after several attempts, infected mice with them. Four lots of ticks were tested in Brussels. Two rats were inoculated with an

emulsion of ticks from Nzulu and one showed spirochaetes on the 16th day. On the other hand two inoculated with ticks from Bogoro remained negative. Professor Roubaud also obtained infection with nymphs reared from *Ornithodoros* collected at Nzulu.

It is evident therefore that Nyangesi, Nzulu, Kisenyi and Géty are centres of spirochaetal infection even though the examination of nearly 500 local inhabitants failed to reveal any signs of infection. The author is of the opinion that these results support the view that the local population of centres of spirochaetal infection acquire immunity against the disease. *E Hindle*

PIROT R. & BOURGAIN M. Non transmission héréditaire de *Spirochaeta persica* Dschunkowsky 1912 chez *Ornithodoros erraticus* [Failure of Hereditary Transmission of *S. persica* in *O. erraticus*] *Bull Soc Path Exot* 1944 v 27 Nos. 1-2 20-23 1 chart. [Summary taken from *Rev Applied Entom Ser B* 1945 June v 33 Pt. 6 92-3]

The usual vector of *Spirochaeta persica* appears to be *Ornithodoros tholozani* Lab & Mégn. but transmission has been effected experimentally by various ticks including *O. erraticus* Lucas. The experiments recorded in this paper were made with a strain of *S. persica* thought to have originated in Persia that has been kept in the laboratory at Toulon for three years is easily maintained in and transmitted by *O. tholozani* and produces only a mild infection in guinea-pigs.

More than 80 examples of *O. erraticus* that had engorged in the second nymphal instar in June 1940 on guinea-pigs heavily infected with this spirochaete failed to transmit the infection to fresh guinea-pigs 7, 8 or 9 months later when they were in the next instar and no infection was seen in any of the rodents on which the ticks were subsequently fed.

CHORINE V & COLAS-BELCOUR J. Sur une souche tunisienne d'*Ornithodoros erraticus* réfractaire à l'infection par *Spirochaeta hispanica* [A Tunisian Strain of *O. erraticus* Refractory to *S. hispanica*] *Bull Soc Path. Exot* 1944 v 37 Nos. 1-2, 24-34 [11 refs.]

RICHTER, C. P. Incidence of Rat Bites and Rat Bite Fever in Baltimore. *J Amer Med Ass* 1945 June 2 v 123 No 5 824-6 2 figs.

In an area of less than two square miles around the Johns Hopkins Hospital Baltimore U.S.A. there are many very poor houses that are infested by the brown rat *Rattus rattus norvegicus*. The rats bite people at night while they are asleep, the great majority of the victims being infants under one year old. Most of the bites treated at the hospital were on the hands, head and feet in that order of frequency.

The house distribution of the bitten persons suggested that the rat, having once tasted human blood, acquires an increased desire for it. An experiment in which rats were offered human blood with an alternative choice of other food and of water indicated that they had a strong preference for blood.

Of 65 persons from this area who were treated at the hospital for rat-bites, seven developed rat bite fever [whether caused by *Spirillum minus* or *Streptobacillus moniliformis* is not stated] *J F Corson*

WHEELER, W. E. Treatment of the Rat Bite Fevers with Penicillin. *Amer J Dis Children* 1945 Apr v 69 No 4 215-20 4 charts. [13 refs.]

Wheeler describes the treatment with penicillin of four cases of rat-bite fever, three due to *Streptobacillus moniliformis* and one to *Spirillum minus*. He has

developed a satisfactory technique for the isolation of *Streptobacillus moniliformis* from the blood—at least 6 cc. of blood are inoculated into 50 cc. of broth, and the culture incubated at 37°C. in an atmosphere enriched with CO₂. The flask is examined daily in a strong cross-light for the presence of "cotton ball" colonies. If present, these are transferred with a pipette to chocolate agar for subculture and to a slide for Gram staining. After incubation in CO₂, the subculture is used to inoculate a plain agar plate and a blood agar plate and to make a smear for staining with Giemsa. The characters required for diagnosis of *Streptobacillus moniliformis* are—typical colonies in broth, Gram-negative pleomorphic organisms in the smear, failure to grow on plain agar and scanty or no growth on blood agar.

Streptobacillus moniliformis was isolated from blood taken from three children—aged 5 weeks, 7 weeks and 6 months—who had been bitten by rats. One of the children showed a marked arthritis, one a fine macular rash, and one showed marked respiratory distress, and later developed an abscess over the sternum from which viable *Streptobacillus moniliformis* were recovered three days after starting penicillin. In two children the temperature was raised, in the third it was subnormal—it returned to normal in all cases 2-4 days after the start of penicillin, though in one child only after three blood transfusions. Penicillin was administered intramuscularly at the rate of 5,000 units every two or three hours for nine days. The clinical progress was satisfactory in all the cases.

A fourth child, aged three months had also been bitten by a rat, was febrile, and showed a macular rash—unlike the other three his local lesions were markedly infamed. His blood did not yield *Streptobacillus moniliformis* on culture but two mice which had been injected with 0.5 cc. showed spirilla morphologically resembling *Spirillum minus* on the 15th day. The response to penicillin, 5,000 units three-hourly was dramatic: the temperature falling to normal in nine hours.

R. E. O. Williams.

YAWS

GUTMARKE, F. N. Boça ("Framboesa" yaws) Tratamento pela penicilina das lesões terciárias: úlceras gomosas, periostites ósteas, áreas de rarefação óssea e gangosa ("Rhino-pharyngitis mutilans") (Nota prévia.) [Penicillin in the Treatment of Tertiary Yaws.] *Brasil-Médico* 1945 Mar 17-24 & 31 v. 59 Nos. 11-12 & 13 89-91 6 figs. English summary.

Brief notes are given of six patients presenting lesions of tertiary yaws—gummata, periostitis, osteitis and gangosa—treated with injections (usually gluteal) of penicillin. The total dosage ranged between 48,000 units given during 20 days to a child of five years with periostitis and 558,000 units over 7½ months to a lad of 16 years with boomerang leg and gummata ulcers. Ten-day rest intervals were given from time to time (36 days altogether in the last case). The treatment in this patient comprised 1,200 units daily for 80 days, 2,400 units for 27 days, 3,600 units for 23 days, 4,800 for 43 days and 9,600 for 10 days.

The gangosa patient was a woman of 28 years. She was given 400 units three daily for six days, then 800 t.i.d. for 39 days then 1,600 similarly for 12 days—altogether 158,400 units [not 164,000 as stated]. The gangosa

cleared up but a residual goundou was observed. Cure was obtained in all cases with ulceration and periostitis but the actual bony changes persisted.

H Harold Scott

CHARTERS, A. D. Foot Yaws. *Trans Roy Soc Trop Med & Hyg* 1945 July v 38 No 6 461-2, 6 figs on 1 pl

A report of a case

LEPROSY

SUÁREZ J. La lepra en Bolivia. [Leprosy in Bolivia.] *Bol Oficina Sanitaria Panamericana* 1944 Nov v 23 No 11 966-74 1 map

In accordance with a resolution passed by the National Antileprosy Service in April 1942 a census of lepers was undertaken in Bolivia. The first team explored the Departments of Beni, Pando and Santa Cruz and they discovered 19 foci and in them 56 lepers and 212 contacts among 6 000 persons examined.

From May to September 1943 a second team was working in six Departments Santa Cruz Beni Cochabamba Tarija Potosí, and Chuquisaca. This second Commission discovered 64 new foci 161 lepers and 497 contacts. Thus the two Commissions found 83 foci, 217 lepers and 709 contacts.

The author then takes each of the Departments in turn naming the foci and the numbers of cases and contacts in each focus. Here it must suffice to give the numbers in the several Departments for reader study the facts presented in the letterpress have been brought together in tabular form.

Department	Foci	Lepers	Contacts
Santa Cruz.	30	70	226
Beni	14	45	132
Tarija	15	33	144
Chuquisaca	16	39	152
Cochabamba	6	22	55

In Chuquisaca there were another six probable foci. As regards Potosí the position is uncertain only one actual patient was seen and he had come from the Province of Charcas. He was isolated in the local hospital but ran away. The information in other respects is quite vague the author stating that 'there are possibly many more cases and several localities may be foci of the disease.

So much for the census aspect. Epidemiological study shows that the foci may be graded active foci are those in which more than 60 per cent. of the cases are florid (*lepra abierta*) stationary where half or less of the cases are of the types L1 L2 or L3 and inactive or becoming extinct where more than 70 per cent. are of the nervous types or *formas frías*. Further analysis showed that 53 per cent were autochthonous 12 per cent imported the source of the remaining 35 per cent. was not known. Ninety two per cent were natives

6 per cent. half-caste and 2 per cent. white. 87 per cent. were males 13 per cent. females. With such small numbers the age-grouping does not convey much information, but the following may be useful —

Age in years	Males	Females
0-4	0	1
5-9	8	2
10-14	13	4
15-19	45	8
20-29	65	3
30-39	33	4
40-49	15	3
50-59	10	3
60-	0	0

The estimated population being taken as 3 000 000 the leprosy incidence is stated to be 70.5 per 100 000. Contact is largely extra-domesticary 77 per cent., as compared with 23 per cent. in the home.

To deal with the situation the Antileprosy Service intends to establish two colonies of agricultural type one in the Michel district where periodic flooding does not occur and medical and other aid can be easily given the other at Los Negros estate in Florida Province. Neither of these is an endemic centre the land is suitable for agriculture water supply is adequate and of good quality and access is by good roads. Next, eight mobile dispensaries are to be provided, each to work in its own determined range. These will continue the census treat the sick, examine periodically the contacts and attend generally to the health education of the people. Propaganda work will also be carried out.

H Harold Scott.

MOURITZ, A. A Brief World History of Leprosy. Hawaii; U.S. America; Philippines, Malaya, Fiji, China, India, Europe. 159 pp. 31 illustrations. Revised 1943. Honolulu, Hawaii. Hawaiian Printing Co. Ltd. [31s 6d.]

MUDROW, Lilly & SCHULTZ, F. Die Rattenlepra unter Vitaminmangel und bei chronischer Sapotoxinveratresung. [The Influence of Vitamin Deficiency and of Prolonged Administration of Sapotoxins on Rat Leprosy.] *Zent. f. Bakt. L. Abt. Orig.* 1943 Dec 11 v 151 No. 1 50-59 3 figs. [10 refs.]

The main part of this paper deals with the effects of vitamin B₂ deficiency on the development of inoculated rat leprosy. The results were largely negative for vitamin deficiency did not appear to increase the generalization of infections with rat leprosy in the case of either B₁, biotin or pantothenic acid, nor was the spread of the rat leprosy bacilli through the system of the animals influenced. No specific effect of the vitamin deficiency on the pathological process could therefore be established, though some general influence may have been exerted in the direction of aggravating the disease. These animal tests may indicate the likelihood of similar influence in human leprosy. The last part of the paper gives data indicating that the supply of sapotoxins to rats infected with rat leprosy does not intensify the severity of the disease.

L. Rogers

HELMINTHIASIS

CAWSTON F G *Bulinus forskalii* (Ehrenburg) as a Factor in the Spread of Schistosomiasis. *South African Med J* 1945 May 12, v 19 No. 9 155

In this note the author emphasises the fact that this snail is to be found in parts of South Africa, and must be taken into account.

SCHWETZ J & DARTEVELLE, E. Le problème des mollusques vecteurs de la bilharziose au lac Albert. [The Molluscan Vectors of Schistosomiasis round Lake Albert.] *Ann Soc Belge de Méd Trop* 1944 June 30 v 24 Nos. 1-2, 58-68 6 figs on 1 pl. [22 refs.]

SCHWETZ J & DARTEVELLE E Répartition géographique des Planorbidæ (*Planorbinae* et *Bulininae*) au Congo belge d'après les collections malacologiques du Musée de Tervuren, 1943 [The Distribution of *Planorbis* and *Bulinus* in the Belgian Congo] *Ann Soc. Belge de Méd Trop* 1944 Sept. 30 v 24 No 3 147-66 3 maps, [10 refs.]

ALMY T P & HARPER J G M Banti's Syndrome apparently due to Infection with *Schistosoma mansoni*. *J Amer Med Ass* 1944 Nov 11 v 128 No 11 703-5 4 figs.

A case of very prolonged development of symptoms the patient being a man of 44 years who had probably contracted his infestation with *S. mansoni* at latest when he was 19 years of age and perhaps earlier. He was an Arab born near Aden in 1899 he had been in the British Navy and the merchant service for five years from the age of fifteen, and since 1919 had not left the United States. Splenomegaly had been observed when he was operated on for hernia at the age of 42. Two months before his present admission to hospital he noticed swelling of his abdomen and legs and shortness of breath on slight exertion. On admission the heart was normal, the liver edge was 7 cm. below the costal margin at the mid-clavicular line and the tip of the spleen was felt at the level of the umbilicus. Blood examination showed red cells 3 600 000 white 4 000 per cmm, with 12 per cent. eosinophiles. Wassermann reaction was negative. After three weeks treatment with iron and liver extract the erythrocytes had increased to 4,900 000 while the leucocytes remained the same in total but eosinophiles were down to 4 per cent. He was then treated with Fuadin but though he tolerated the drug well it had no effect on the liver or spleen which 10 weeks after cessation of treatment, remained the same as before. There seems to be no doubt that infestation had occurred at his place of birth which he had left 30 years ago. [It is true that no other cause was found to account for the enlargement of the liver and spleen but the tissue of neither organ was examined by biopsy and, on the other hand nothing certain is known regarding the aetiology of Banti's syndrome. It would perhaps be safer to call this a long-standing case of Schistosomiasis mansoni associated with the signs and symptoms of Banti's syndrome.] H Harold Scott

ALVES W Intensive Treatment of Schistosomiasis with Antimony (Preliminary Note.) *South African Med J* 1945 May 26 v 19 No 10 171-2.

The author was led to make trial of this method of intensive treatment first, because of the reported success of a similar method with arsenic in syphilis and secondly because schistosomiasis is a very important problem in Southern Rhodesia. He used a preparation of sodium antimonyl tartrate (S.A.T) in

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H. Harold Scott

MOOREHEAD, A. A Brief World History of Leprosy. Hawaii, U.S. America, Philippines, Malaya, F.M.S.; China, India; Europe. 130 pp. 31 illustrations. Revised 1943. Honolulu, Hawaii. Hawaiian Printing Co. Ltd. [31s. 6d.]

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ampoules containing 1 or 2 grams and the injection was made up to 10 cc. with 5 per cent. glucose saline. The calculated dose was approximately 12 mgm. per kilo body-weight, and was administered in 7-8 doses over a period of 30 hours with 16-18 hours break after the first day of treatment. For example, a young adult weighing 55 kgm. was given 650 mgm. as follows: 65 mgm. at 9.30 and 11.30 a.m. and at 2 p.m. 130 mgm. at 4.30 p.m. At 8.30 a.m. next day (i.e. after a 16 hours interval) 130 mgm. at 10.30 a.m., 12.30 and 3.30 p.m. 63 mgm. each time the whole being thus spread over 30 hours. Each intravenous injection was given slowly 5-6 minutes being taken over it. Reports of the results have so far been very good and most encouraging. The ova disappeared or if found, were not viable, after a couple of days. Brief notes of five patients are given and a reference to a sixth who has been lost sight of. It may as the author acknowledges be too soon to claim a cure, for a longer follow-up is needed, but the method in his hands has had no troublesome complications and is well worth, and will doubtless receive, more extensive trial.

H. Harold Scott.

VIDELA C. A. & SCODELLER J. A. Diatomatosis Hepatica. [Infestation with *Pastoria brevis*. An Pobl. Enf. Infecciosas del C. A. i. de la Hospital F. J. Muñoz Buenos Aires. 1942-44 No. 4, 144-63 1 fig. English summary (3 lines)]

APPLEBAUM, L. L. & WEINBERG, L. E. Eosinophilia in Cerebrospinal Fluid. *J. Amer. Med. Ass.* 1944 Mar 25 v. 124 No. 13 830-31 1 chart. [17 refs.]

"1. A case with the findings of eosinophilia in the spinal fluid and manifestations of acute cerebrospinal meningitis was observed.

"2. The syndrome closely resembled cases of cysticercosis of the central nervous system previously described and was considered the most probable diagnosis.

"3. The condition is more common than is generally recognized and in suspected cases such special procedures as sedimentation of the spinal fluid in a search for eosinophils and intradermal and precipitin tests are recommended."

[Seventeen references are given to the literature of this subject.]

SELMAN D. Eosinophilia in Cerebrospinal Fluid. Report of Case. *Bull. U.S. Army Med. Dept.* 1945 Mar No. 86 121-2, 1 fig.

The patient was a man with signs of meningeal irritation, and slight fever. On the day after admission the blood showed 5 per cent. of eosinophils in a total leucocyte count of 7,400 per cmm. and the blood eosinophils never exceeded 5 per cent. during the illness. On the day after admission the cerebrospinal fluid was hazy and colourless with a pressure of 12 mm. Hg. it contained 480 cells per cmm. of which 71 per cent. were eosinophils and 27 per cent. were lymphocytes. The Wassermann and colloidal gold tests were negative. On the third day there was no nuchal rigidity and the cerebrospinal fluid showed 670 cells per cmm. with 78 per cent. of eosinophils. On the 21st day it showed only five cells per cmm. of which one was an eosinophil. On the 13th day the subject was discharged to duty. The treatment is not described.

Examination of the stools for parasites at intervals were all negative. The author refers to literature recording the following causes of cerebrospinal eosinophilia: neurosyphilis "experimental serum meningitis" "therapeutic

He concludes that cerebral cysticercosis was the most likely cause of the eosinophilia observed in this subject but lack of antigen prevented intradermal precipitin and complement fixation tests for the detection of this parasite or of *Echinococcus*. The fact that the illness came on six days after the last of three prophylactic injections with typhus fever vaccine suggests to the author that these injections might cause cerebrospinal eosinophilia and he suggests that this problem should be investigated. [See also this *Bulletin* 1942 v 39 705]

G Lapage

HOWORTH M B. Echinococcosis of Bone. *J Bone & Joint Surgery* 1945 July v 27 No 3 401-11 7 figs. [75 refs.]

The development of our knowledge of echinococcus disease has been outlined and its etiology and distribution have been described. The disease is rare in this country but not uncommon in other areas and its increase may be expected because of conditions growing out of the War. Its diagnosis especially in bone is not difficult if its possibility is realized, and if proper laboratory tests and roentgenograms are made. Treatment has been unsatisfactory to date. Marsupialization or sterilization of the cyst sometimes may be successful. Roentgen radiation has failed. Removal of the entire diseased area has removed the disease but is mutilating. Insertion of bone chips will not be successful unless the disease has been eradicated.

LISBÔA A. Estrongilose renal humana. [Renal Strongylosis in Man] *Brasil-Médico* 1945 Mar 17 24 & 31 v 59 Nos 11 12 & 13 101-2.

Infestation of man by *Dioclophyma renale* is exceedingly rare. Only nine cases have been recorded before this. The patient was a white woman, 54 years of age a resident of Maranhão a Province of Brazil who had suffered from pruritus vulvae for the past nine years. Suddenly one day during micturition she felt a stoppage as if a stone had blocked the urinary passage on straining the flow returned and a worm was passed. There has been no further trouble and the pruritus has ceased. The worm was sent for examination to Dr Carlos Porto who diagnosed it as a male *Dioclophyma renale* [*Eustrongylus gigas*]. This is the largest of the parasitic nematodes the female may attain a length of 3 feet and the thickness of a man's finger the male is only one-fourth to one-third the length of the female. The life-history is not known the infestation is more commonly found in dogs and is thought to be acquired by ingestion of raw fish.

H Harold Scott

TSUCHIYA H & RELLER Helen. A Case of *Trichostrongylus* Infection with Notes on the Identification of Ova. *J Lab & Clin. Med* 1945 Mar v 30 No 3 262-6 1 fig

Infestation with *Trichostrongylus* is exceedingly rare in the United States but in India it has been reported in 9-25 per cent of the population of the sheep- and goat raising areas [this *Bulletin* 1942 v 39 775] and in Japan in 32.3 per cent. [see also this *Bulletin* 1937 v 34 457 and 1939 v 36 845]

The authors now report the finding of *Trichostrongylus* eggs in the faeces of a man who died of malignant disease in the United States. Attempts to culture the worms were unsuccessful so that the species could not be determined.

Discussing the identification of the eggs of *Trichostrongylus* the authors describe them as being much longer and slightly wider than those of hookworms which they may resemble. A table of measurements of 25 *Trichostrongylus* eggs shows that they measured 81-97 microns long by 40-51 microns broad average

86 by 43 microns. The shell membrane of the *Trichostrongylus* eggs is thicker and more greenish and lustrous than that of hookworm eggs. MAPLESTONE (this Bulletin 1942, v 39 775) likened their shape to that of the eggs of a bird. In fresh stools *Trichostrongylus* eggs show advanced segmentation of the contents 16 to 24 cells usually being present. *Haemonchus contortus* is another rare parasite of man and its eggs may cause confusion. They cannot be distinguished from those of *Trichostrongylus* and the only method of identifying this species is by cultivating the infective larvae or by finding the adult nematode. The eggs of *Strongyloides stercoralis* may also be found, but these are smaller and have a thinner shell membrane which is less greenish and less lustrous. In the fresh stool the eggs of this species contain an embryo.

The eggs of *Heterodera radicicola* may appear in human stools after ingestion of vegetables in which this nematode is parasitic. The eggs of this species have a unilateral flattening or a slight concavity and their ends are rounded but distorted eggs may be incorrectly diagnosed. They may disappear when the subject is put on a diet free from vegetables.

The authors stress the importance of careful stool examinations for the differentiation of the eggs of *Trichostrongylus* from those of the hookworms.

G. Lapege

CRAM E. B. & HICKS D. O. The Effect of Sludge Digestion, Drying and Supplemental Treatment on Eggs of *Ascaris lumbricoides*. *Proc Helminth Soc. Wash.* 1944 v 11 1-8 [Summary taken from *J. Nat. Bur. Health* 1945 May v 15 No 5 156 Signed T. E. Gibson]

Eggs of *A. lumbricoides* originating from man and swine were introduced into sewage taken from a town main and the sewage seeded with ripe sludge generally in the proportion of four parts of settled sewage to one part of ripe sludge. To ten parts of ripe sludge was added daily for 30-60 days one part of fresh settled sewage giving a yield of 60-72 litres of sludge at the end of the observation period. The effects of digestion were observed for 2-6 months and then the sludge was poured for drying into wooden frames containing layers of gravel and sand of varying depths. The different lots of sludge were dried by exposure to constant temperatures of 86° and 68°F and to the varying temperatures of the laboratory, a greenhouse and a porch roof. Viability of the eggs was judged by the development of active embryos.

Eighteen lots of eggs were placed in digesting sludge and practically none developed. The eggs were very resistant to the digestive process and an average of 70 per cent. of all eggs exposed at different temperatures were viable during the first three months, after which a sharp drop in viability occurred. At the end of six months however about 10 per cent. of the eggs were still viable. Repetition of the sludge digestion appeared to be no more deleterious to *Ascaris* eggs than was continuous sludge digestion. It was found that under the aerobic conditions found in activated sludge active embryos developed in *Ascaris* eggs which had been unsegmented when they were introduced into the sewage. Subsequent exposure to anaerobic sludge digestion showed that embryonated eggs survive anaerobic digestion for periods longer than those usually allowed for sludge digestion, although they seem to be less resistant than non-embryonated eggs.

Six lots of digested sludge were dried in the greenhouse and 13 cakes of sludge were dried outside. Variable viability was noted under these varying conditions but it appears that *Ascaris* eggs cannot survive a reduction of moisture content to below 5 per cent. Storage of pulverized, dried sludge containing 30.7 per cent. of moisture at 68°F in a tightly covered glass dish did not influence the viability of *Ascaris* eggs during 44 days. Subsequently the powdered sludge

was left in a loosely covered dish which allowed slow drying and 71 days later the moisture content was 4.5 per cent. and no viable eggs could be recovered. Heating the sludge to 50°C. for 20 min. killed about 50 per cent. of the viable eggs present and heating to 103°C killed all the *Ascaris* eggs present. Fumigation of eggs in sludge and sand with methyl bromide for 24 hours destroyed those eggs which had not started their development but had little effect on partially or completely developed eggs.

ENGLEHORN T D & WELLMAN W E. Filariasis in Soldiers on an Island in the South Pacific. *Amer J Med Sci* 1945 Feb v 209 No 2 141-52 4 figs

An account is given of the early symptoms and signs of illnesses which were diagnosed as filariasis occurring among American soldiers stationed in an island in the eastern part of the South Pacific Ocean. Neither adult nor larval filariae were found in the patients but filariasis was very common among the natives of the island there was close contact between the troops and the natives and the commonest mosquito present in great numbers was *Aedes scutellaris*.

The shortest period between possible exposure to infection and the development of symptoms was 3 months mild symptoms appeared most frequently after 5 months and severe symptoms after 8 months.

The earliest symptoms were malaise insomnia, anorexia, nausea vomiting and pain in various parts of the body after about 2 weeks pruritus, tenderness and swelling of the scrotum and spermatic cord developed and in some patients signs of acute lymphadenitis and acute lymphangitis appeared usually in the upper arm and the thigh and spread peripherally.

All the patients had funiculitis 69 had orchitis and 22 had epididymitis while lymphadenitis was present in 9 acute lymphangitis in 8 and acute cellulitis in 9. Some of the patients had transient soft, non-suppurative swelling in the arm hand leg or upper eyelid.

In accordance with the policy of the Army the men were evacuated to the U.S.A.

A short account illustrated by photographs is given of filariasis among the natives
J F Corson

GERMAN W M. Observations on the Microfilaria of *Onchocerca volvulus* with Silver Stains. *Amer J Trop Med* 1945 Mar v 25 No 2 129-36 8 figs.

The illustrations of the larvae of *Onchocerca* in recent textbooks are criticized their lack of detail being due in the author's opinion to the use of routine stains he has found that a silver staining method gives a better contrast between the larvae and their surroundings and shows more anatomical detail.

The following watery solutions are used (a) 2 per cent. AgNO_3 (b) ammoniacal silver carbonate prepared as follows—to 5 cc. of 10 per cent. silver nitrate add 15 cc. of 5 per cent. Na_2CO_3 then add strong ammonia solution drop by drop until the white precipitate is dissolved and add a few extra drops then add distilled water to 75 cc (c) 1 per cent. formal (d) 5 per cent. sodium hyposulphite

Frozen sections are placed successively in the following (1) distilled water (twice) (2) in (a) and heat at 60-70°C until the sections become faintly yellow (15-20 minutes) (3) distilled water (twice) (4) in (b) for 3-5 minutes (5) distilled water for 1 minute (6) in (c) for 1 minute (7) distilled water (8) in (d) for 1 minute (9) distilled water drain blot dehydrate clear in creosote, and mount in clarite x. The larvae are stained black in a yellow background.

The author discusses the morphology of the larvae as shown by this silver method and describes their position in the nodules—he concludes that they leave the nodule by the perivascular spaces. [The morphology of the larva of *O. rostratus* is well shown in a paper by FULLERSON and SIMON *Arch. f. Schiffs u. Tropenhyg.*, 1913 v 17 Beihft 9 (see this *Bulletin* 1914 v 3 100)]

J F Corson.

ROUTHAIN J Contribution à l'étude des ganglions inguinaux dans l'adénolymphocèle et l'éléphantiasis du scrotum au Congo Belge. [The Inguinal Glands in Adenolymphocèle and Elephantiasis in the Belgian Congo.] *Ann. Soc. Belge de Méd. Trop.* 1943 June 30 v 23 No 2, 91-111 6 figs. [10 refs.]

In a previous paper (*Ann. Soc. Belge de Méd. Trop.*, 1938 v 16 253) the author described the histological appearances of lymphatic glands removed from African natives of the Belgian Congo who were infested with *Onchocerca rostratus*: two of those patients had adenolymphocèle and one had scrotal elephantiasis. In the present paper detailed descriptions are given of the conditions observed in lymphatic glands and pieces of skin excised from Congolese natives with "adenolymphocèle" or scrotal elephantiasis. Some of the specimens came from Niangara in the Uele area where nearly the whole of the population has onchocerciasis, while others came from Coquilhatville, where onchocerciasis exists but is less common.

The glands and skin showed fibrosis of varying degree, especially in cases with onchocerciasis—in some glands the lymphatic channels were dilated but no large spaces were seen. The author thinks that further observations with more associated details are needed and that comparisons should be made between these cases in Central Africa and similar conditions associated with filariasis caused by *Wuchereria bancrofti*.

The meaning of the term "adenolymphocèle" is discussed. STEPHENS and YORKE ("The Practice of Medicine in the Tropics" by BYAM and ARCHIBALD 1923 v 3 1928) are quoted as stating that it "apparently implies dilatation of the sinuses in a lymphatic gland." DUBOIS (*Bull. Acad. R. de Méd. de Belgique* 1940 VI ser v 6 364) regards it as an unsuitable term, and the author thinks it is used for more than one pathological condition.

J F Corson.

BELL, S. D. JR & BROWN H. W. Studies on the Microfilarial Periodicity of *Litomosoides carinii* Filariid Parasite of the Cotton Rat. *Amer. J. Trop. Med.* 1945 Mar v 23 No. 2 137-40 3 figs.

Litomosoides carinii, a filarid parasite of the thoracic cavity of the cotton rat *Sigmodon hispidus* and of various other rodents, appears to have been given various names. *Filaria carinii*, *F. peterseni*, *Litomosoides sigmodontis* and *Micropleura sigmodoni*.

The authors examined thin blood smears stained with alum haematoxylin and observed the following characters: the microfilaria has a sheath about 100 μ long, a clear area behind the anterior end of about 3-5 μ and the nuclei reach to the end of the tail in most cases.

Thick smears were made with 3.5 cmm. of the tail blood of six cotton rats every four hours for 48 hours, and stained with Giemsa's stain, and the microfilariae were counted. Although considerable variations in numbers were found there was no obvious nocturnal or diurnal periodicity. To determine whether there was any periodicity over longer periods one rat was examined every 12 hours for nine days and every 24 hours for 20 days: no regular cyclical variation was found.

The considerable variations which occur make this filaria difficult for testing the effects of chemotherapy but for testing the killing power of drugs on the adult filariae the cotton rat is a good experimental animal [see this *Bulletin* 1944 v 41 772 1945 v 42 136] J F Corson

RODHAIN J Présence de *Microfilaria streptocerca* dans les régions de Lisala et de Basankusu (Congo Belge) [*Microfilaria streptocerca* in the Belgian Congo] *Ann Soc Belge de Méd Trop* 1943 Sept-Dec. v 23 Nos 3-4 203-8 6 figs on 2 pls.

Agamofilaria streptocerca was found in 1939 in the skin of three natives of the Belgian Congo two of the natives were in Lisala and one in Basankusu. This larval form was also found in Nepoko in the Belgian Congo in 1938 by DUBOIS and VITALE [this *Bulletin* 1940 v 37 306] J F Corson

DEFICIENCY DISEASES

BRIGGS A P SINGAL S A & SYDENSTRICKER V P A Study of Nicotinic Acid Restriction in Man. *J Nutrition* 1945 May 10 v 29 No 5 831-9 1 fig [20 refs.]

Two subjects each of whom previously had been a pellagra patient restricted themselves to a diet low in trigonelline and providing only about 3 mg of nicotinic acid daily one for a period of nine weeks and the other for 42 weeks.

Each had minimal lesions of nicotinic acid deficiency at the start but in neither was there any significant development in the direction of pellagra.

The nicotinic acid excretion of one remained low throughout the study the other remained at a normal level.

The trigonelline output in each case dropped to a low level within 3 weeks but showed no tendency to fall to a lower level with prolonged restriction.

Niacin tolerance tests in each case were interpreted to indicate a mild state of deficiency.

Tests for the fluorescent substance F_2 were zero at the start as well as at the close of the periods of restriction.

It is suggested that the failure in the development of pellagra may have been due possibly to intestinal biosynthesis of nicotinic acid and possibly to the fact that the diet contained little corn.

Apparently under the conditions of our study the 3 mg daily of the diet provided an intake somewhere near the minimal niacin requirement.

RACHMILEWITZ M & BRAUN K Electrocardiographic Changes and the Effect of Niacin Therapy in Pellagra. *Brit Heart J* 1945 Apr v 7 No 2 72-80 4 figs [13 refs.]

The authors (writing from Jerusalem) produce further observations upon electrocardiographic changes in patients showing clinical signs of nicotinic acid deficiency which were eliminated by the administration of this substance but not by vitamin B₃. Of the 27 subjects 22 had typical skin lesions of pellagra 10 showed as well evidence of thiamin deficiency such evidence according to the authors being pains in the calf muscles paraesthesia muscular weakness and cramps as well as objective findings indicating peripheral neuritis but not one patient had disturbances of cardiac function and none a beriberi.

heart. [Here the authors do not seem to be very clear—the one condition which is due to a thiamin deficiency is the beriberi heart, while the relationship between the so-called peripheral neuritis and vitamin B₁ is doubtful.]

The changes in the E.C.G. considered to be due to nicotinic acid deficiency (16 cases) were alterations of the final deflection of the ventricular complex—alteration of the S-T segment or of the T wave, since though similar changes may be seen in beriberi, arteriosclerosis myxoedema, etc. they appeared to clear up after the exhibition of 300 to 500 mgm. of nicotinic acid per diem. None of these cases showed any clinical or radiological evidence of cardiac abnormality.

In two cases in which there was an associated protein deficiency the condition did not respond until the blood protein had been restored to normal. Nine cases showing well marked dermal manifestations of pellagra without obvious signs of involvement of visceral organs tended to give normal E.C.G.

H. S. STARRIS

COMENFORD C & KIRMAN B H Pellagra in a Morphine Addict. *Brit Med J*
1945 July 14 44-5

CARLEY P S History of Pellagra in the United States. *Urologic & Cutaneous Rev*
1945 May v 49 No 5 291-303 [147 refs.]

HAEMATOLOGY

INDIA. ARMY PATHOLOGY ADVISORY COMMITTEE GENERAL HEADQUARTERS (INDIA) Report on Investigations on Anaemia in the Indian Soldier from the Anaemia Investigation Team General Headquarters (India) September 1943-January 1945 [HYNES M Officer in Charge] 59 pp 18 figs. [52 refs.] 1945. New Delhi Printed by the Manager Government of India Press.

Anaemia in the Indian soldier was a major medical problem on the Indo-Burma front during 1943. An investigation into the cause of this anaemia was undertaken between September 1943 and January 1945.

The first section of the report gives a review of the literature on anaemia in India. Over fifty papers, to which the references are given, have been consulted. It is a useful summary.

Haemoglobin surveys of several groups of soldiers, pioneers and recruits were carried out. A haemoglobin level of not less than 14 gm. per 100 ml. was taken as "satisfactory" and one of less than 11 gm. as indicating anaemia of a sufficient degree to justify hospitalization. Two intermediate groups were also recognized, "doubtful"—13 to 13.9 gm. and "mild" anaemia—11 to 12.9 gm.

The reviewer has tabulated the findings (below) the percentages are calculated to the nearest whole figure.

The possible causes of the relatively low haemoglobin in most of the Indian groups is discussed. The effects of hookworm infection, dietary deficiency, malaria, length of service and altitude are considered. Statistically significant evidence for the effect of hookworm infection is found, but the authors of the report are disinclined to give this infection the importance it appears to deserve for several reasons that are stated. [The reviewer questions the validity of

	Percentage in each group				
	No of persons	Anaemic	Slightly anaemic	Doubtful	Satisfactory
<i>Imphal area (3 000 to 10 000 feet)</i>					
Madras Pioneers	100	17	29	24	30
Bengal Pioneers	60	0	3	5	92
British other ranks	200	1	6	14	80
Mahrattas & Jats	500	2	8	12	78
Gurkhas	210	5	22	25	48
Patiala Brigade	100	7	24	29	40
<i>Peshawar District (1 100 feet)</i>					
North West Indians					
February	1 119	8	32	33	30
May	189	3	8	25	63
Madras	200	1	27	36	37
Brit. other ranks	195	0	9	32	60
<i>Lands Kotal (3 500 feet)</i>					
Punjabis	197	2	17	28	53
Bhairab Natha	200	1	3	19	76
Kashmiris	200	2	5	14	80
<i>Rawalpindi</i>					
Recruits	600	7	19	19	55

excluding hookworm infection as the cause of anaemia because of the absence of (i) demonstrable hookworm infection in certain anaemic individuals of a hookworm-infected group and (ii) anaemia in some relatively heavily infected persons.] The longer the service the less the anaemia, but this fact may of course also be correlated with hookworm infection.

A more detailed blood examination of recruits was made and it was found that the anaemia was mostly of the ortho or hypochromic types.

It was found that iron administration raised the haemoglobin level often to a remarkable degree in all the substandard groups and in most of the individuals of these groups even when the haemoglobin percentage was previously satisfactory. Iron was given in the form of ferrous sulphate (exsiccatus) suspended in water in doses of 18 to 20 grains daily for 14 to 21 days.

The haemoglobin level of most recruits improved remarkably during their first three months of army life but if iron were also given the improvement was even more striking.

The authors conclude that one of the main causes of anaemia is a low iron reserve in the recruit which the ordinary army diet is not able to supplement sufficiently. They therefore recommend that all recruits be given 6 grains of ferrous sulphate daily during their training. [Blanket administration of iron to tea-garden coolies has always caused an improvement in their haemoglobin level and general health and if the authors' recommendation is put into practice it will probably be very beneficial to the health of the Indian Army.]

The report includes over fifty tables of haematological data. Its value is considerably enhanced by the systematic statistical criticism.

L. E. Napier

LURIE H. I. Normal Haematological Standards at an Altitude of 5,470 Feet (Witwatersrand, South Africa.) *Quart. J. Exper. Physiol.* 1945 May v 33 No 2, 91-105 5 figs [23 refs]

The subjects providing the material for this investigation were healthy European residents of the Witwatersrand. They numbered thirty of each sex and their ages ranged from eighteen to forty years.

Venous blood was used for the determination of the absolute indices. The haemoglobin estimations were performed with a Klett Summerson photo-electric colorimeter which had been carefully calibrated by a variety of methods. The more important results, expressed as mean figures, were as follows. Red cell count per cmm males 5,593,000 females 4,999,000 Haemoglobin gm per 100 cc males 17.76 females 15.33 MCV males 89.58 cc females 90.42 cc. MCH males 31.69 μ females 30.65 μ M.C.H.C. males 33.47 per cent females 33.82 per cent.

It is noted that these figures show a significant elevation both of the red cell count and of the haemoglobin concentration compared with figures usually accepted as normal at sea level. The rise in the haemoglobin is in conformity with Fitzgerald's law which states that the haemoglobin rises 10 per cent for every 100 mm. mercury fall in barometric pressure.

Comparing these results with those of previous investigators on the Witwatersrand the author points out that although the latter show raised red cell counts comparable with his present figures the haemoglobin readings previously reported were similar to or lower than those considered normal for sea level. He is satisfied that this discrepancy may be entirely explained by the difference in the type of haemoglobinometers used by the earlier workers.

L. J. Davis

HURTADO A. MERINO C. & DELGADO E. Influence of Anoxemia on the Hemopoietic Activity *Arch. Intern. Med.* 1945 May v 75 No. 5 284-323 22 charts [Refs. in footnotes]

This paper records work performed in Peru mostly at high altitudes. Very thorough haematological studies including blood volume and oxygen saturation determinations, were performed on a series of healthy men both at the sea level and at varying altitudes up to 15,660 ft. The subjects studied also included aviators, train crews on Andean railways, Indian natives living at high altitudes and patients with pneumoconiosis.

The conclusions may be summarized as follows —

Exposure to low barometric pressure causes in most cases a polycythaemic response which at high altitudes is absolute in type, the total blood volume being elevated as a result of the increased red cell volume. There is also a proportional elevation in the circulating reticulocytes and in the serum bilirubin. It is thought that this latter feature suggests an increased rate of red cell destruction running parallel with the increased production.

Leucopoietic activity is not affected, a temporary leucocytosis which is occasionally observed on first arrival at a high altitude, being thought to be due to a release or mobilization of stored blood.

Chronic anoxaemia does not modify erythropoietic activity permanently since when a native of high altitudes is brought down to the sea level, his blood characteristics eventually resemble those normal in persons living at this level. During the early period of adaptation to normal pressure however there frequently occurs an abnormal decrease in the red cells and haemoglobin.

There appears to be a limit for the haemopoietic response to anoxaemia for when this is extremely severe a decrease rather than a further increase is observed in the resulting polycythaemia, which is attributed to an interference

with the formation of haemoglobin. The polycythaemia of high altitudes was compared with polycythaemia observed in individuals living at sea level and it was concluded that in the latter category when anoxaemia was due to pulmonary disease the polycythaemia tended to be of lesser degree than with a corresponding degree of arterial oxygen unsaturation at high altitudes. It is also considered unlikely that the causative mechanism of polycythaemia vera is related to the existence of an anoxic stimulus.

L J Davis

NEUDA P M & ROSE M S Preliminary Report on a Rapid Method for diagnosing Sickie-Cell Disease. *J Lab & Clin Med* 1945 May v 30 No 5 456-8

This new rapid method for the diagnosis of sickle-cell anaemia and sickle-cell trait is performed as follows.

A cherry sized quantity of formed human faeces is rubbed up in 5 cc of normal saline and filtered. 0.1 cc of the filtrate is transferred to 5 cc of normal broth and incubated for 24 hours at 37°C. A drop of the resulting ferment broth is then gently mixed on a slide with a droplet of the suspected blood covered with a cover-slip and examined microscopically. In a positive case the appearance of sickling regularly occurs in less than an hour.

The ferment broth may be kept at room temperature or in the refrigerator but it must be renewed every few days by subculturing into normal broth.

The authors claim not only that the test is invariably positive in cases which show sickling in ordinary sealed wet preparations but that it is more sensitive than the ordinary methods.

They attribute the mechanism of the test to the presence of an enzyme-like factor in the broth which initiates the process of sickle-cell haemolysis in susceptible cells and suggest that this factor may be related to the blood group ferment of SCHEFF and BOYD (*Blood Grouping Technic* New York N.Y. 1942 Interscience Publishers Inc. p 182).

L J Davis

TROWELL H C Sickie-Cell Anaemia. *East African Med J* 1945 Feb v 22 No 2 34-45

Most of the reports of cases of this condition relate to patients of African descent in the U.S.A. relatively few cases having been described in Africa. The present communication comprises a detailed description of a number of cases seen by the author amongst Bantu tribes native of Eastern Central Africa.

The author confirms that the condition is hereditary, being a Mendelian dominant and manifests itself chiefly in infancy, many patients dying before adult life. Detailed clinical and haematological findings are described in a number of cases and post mortem findings in two. It is emphasized that the presence of nucleated red cells in the peripheral blood of an African should always suggest sickle-cell anaemia and that no blood count of an African can be considered complete unless a sealed drop preparation is made and examined for sickle cells.

L J Davis

VALENTINE W N & NEEL J V The Artificial Production and Significance of Target Cells. With special reference to their Occurrence in Thalassaemia (Cooley's Erythroblastosis Anemia). *Amer J Med Sci* 1945 June v 209 No. 6 741-52, 3 figs. [13 refs.]

PAPPENHEIMER, A. M. THOMPSON W. P. PARKER D. D. & SMITH Katharine E. Anaemia associated with Unidentified Erythrocytic Inclusions, after Splenectomy *Quart. J. of Med. (n.s.)* 1945 Apr. v 14 No. 54 75-100 17 figs on 5 pls. [19 refs.]

A careful study is presented of peculiar erythrocytic inclusions that were seen in the peripheral blood of three patients after splenectomy.

The patients, whose ages were 20, 23 and 33 years, were unrelated white Americans living in the Eastern States, with no history of tropical residence. In each case the presenting complaint was severe anaemia of rapid onset accompanied by splenomegaly. In two cases the anaemia was haemolytic in type but was not relieved by splenectomy or other measure and terminated fatally. The autopsy findings are described in detail. In the third case the anaemia was less severe and also was not significantly affected by removal of the spleen.

In all cases the erythrocytic inclusions were first noted shortly after the splenectomy and were present in all subsequent blood examinations. The affected red cells, which, on an average, constituted 25 per cent. of the total, were seen, in blood films stained with Wright or Giemsa, to contain 1 to 20 or more coccoid or bacillary-shaped inclusion bodies. The bodies were readily distinguishable from the granules of basophilic stippling and from Howell-Jolly bodies. Their staining reactions were positive for iron, but negative with the Gram and Feulgen methods. Attempted culture of the blood in one case was unsuccessful, but cultures in Giemsa's medium from the spleen of the same patient yielded a growth, which could be subcultured on to agar of small pleomorphic organisms morphologically resembling the bodies seen in the peripheral blood, but giving a negative iron reaction and failing to agglutinate with the patient's serum. Inoculations of this culture material into a variety of animals, some of which were splenectomized, and into developing eggs were all negative. The significance of this organism was thought to be highly doubtful.

The possible relationship of these inclusions to various known blood parasites such as *Bartonella Haemobartonella Eperythrozoon* and *Anaplasma* is discussed at length. It is concluded that no definite proof of their parasitic nature has been obtained, and consideration is given to an alternative interpretation that they are identical with the siderophil granules described by GROENEBOG.

[This somewhat lengthy and well illustrated paper should be consulted in the original by all interested, since it is impossible to deal with it adequately in a short abstract. It bears the imprint of careful and competent investigators, and clearly indicates that close attention should be paid to the morphology of the blood cells of patients whose spleens have recently been removed, for if these inclusion bodies are living organisms it would be strange if their topographical distribution were confined to the New York area. Moreover if, as seems more probable, the inclusion bodies are products of disordered haemoglobin metabolism, the phenomenon is obviously one requiring further investigation.]

L. J. Davis

MAXX L. The Preparation of Dehydrated Liver *East African Med. J.* 1945 Jan., v 22, No 1 21-4

The details are given of a new type of dehydrated liver preparation manufactured in East Africa. The final product is a fine granular powder of which 1 lb. is derived from 4 lb. of raw liver. To prevent the danger of rancidity and deterioration owing to the presence of fats, the preparation is packed in evacuated and hermetically sealed tins. This substance differs from other liver preparations in that it contains the whole of the liver protein unchanged, and

accordingly in addition to containing the medicinal properties of liver it should be valuable as a food.

L. J. Davis

TROWELL, H. C. The Treatment of Anaemia in Africans with special reference to a Trial of Dehydrated Liver *East African Med J* 1945 Jan. v 22 No 1 15-20

This paper discusses some of the puzzling points regarding the aetiology and nature of nutritional macrocytic anaemia seen by the author in Africans in Uganda. It is noted that in his experience the administration of beef and of food in large amounts is disappointing therapeutically. Although the patients were found to respond satisfactorily to massive dosage with the cruder liver extracts the expense of this treatment is considerable. Feeding with whole liver is not always possible because of the difficulty of obtaining it in adequate amounts.

The dehydrated liver preparation described by Mann [above] which was manufactured in Kenya was found to be of great therapeutic potency in the treatment of these cases. In a daily dosage of 2 oz. it was more active than cooked liver in daily doses of half a pound and thus appeared to provide an excellent and cheap form of treatment.

L. J. Davis

VENOMS AND ANTIVENENES

WALKER C. W. Notes on Adder-Bite (England and Wales) *Brit Med J* 1945 July 7 13-14 1 graph.

Three years ago the author published in the *British Medical Journal* a request for information regarding bites by the adder (*Vipera berus*) in Britain. His notes here are based on accounts of 50 persons so bitten. He presents a graph of 30 of them which shows that most cases occur in June (8 cases) next May and August (5 each) July (4) April and September (3) March and October (1) that is oftenest in the hot months. Most were on the hand. The symptoms need not be detailed, they were those of viperine poisoning well known to readers of this *Bulletin* but comprised briefly local pain haemorrhagic oedema dilated pupils faintness giddiness and varying degrees of collapse with pallor cyanosis sweating and loss of consciousness partial or complete. Recovery was usually complete but might be slow with residual pain and stiffness for several weeks. Some patients reported after-effects but except for one who shed all his finger- and toe-nails a year after being bitten [the site is not stated] these had probably little connexion with the original bite. The author states that there have been seven fatal cases in the last half-century and mentions five of them the youngest was a child of three years dying in six hours another 4½ years (death in 60 hours) the third, a girl of six years in delicate health (36 hours) another also delicate aged 11 years (12 hours) and the last an insane adult who lived for 28 hours after being bitten. None of these had been given antivenene.

H. Harold Scott

CILLI V. & CORAZZI G. Studio sugli antigeni del veleno di *Echis carinatus* eritreo e sui corrispondenti anticorpi. [On the Antigens of the Venom of *Echis carinatus* in Eritrea and their Corresponding Antibodies.] *Boll Soc Ital. di Med e Igien Trop* (Ser. Eritrea) 1944 v 4 No 4 641-83 [52 refs.] English summary

[This is an important and valuable article and contains so much information that the ordinary reader must study it again and again if he hopes to absorb

it all. In the opinion of the abstracter it would have served its purpose better if the whole had been divided up and the information published in a series of papers or on the other hand the sections might be amplified and the whole issued as a separate monograph. To deal adequately with the article would fill several pages of this *Bulletin*—hence only the main points can be referred to and those interested must consult the original for details.]

For all the experiments recorded the dried venom kept *in vacuo* and in the dark has been used—diluted with sterile saline for the dosage needed.

First, the toxicity of the venom for laboratory animals was determined by intravenous and subcutaneous injection into rabbits guinea-pigs and mice. The results show some peculiar differences [to which, however the text makes no reference]. For example 0.01 mgm. per kilo body-weight intravenously injected will kill rabbits in 10–15 minutes and 0.02 mgm. in 2–5 minutes. But for guinea-pigs, 0.08 mgm. per kilo is needed to cause death in 10 minutes (or eight times the amount needed for rabbits). Subcutaneous injection of 9–10 mgm. per kilo was needed to cause the death of a rabbit in 12–24 hours, whereas for guinea-pigs 0.36–0.48 mgm. killed in 27 hours to 5 days—nearly one thirtieth the dose for rabbits. Mice [weight not stated] required 0.2 mgm. intravenously to cause death in an hour or so and 0.1 mgm. killed in 3–4 hours subcutaneously. 1 mgm. killed in 2 hours. 3–4 mgm. in 1½ hours and 1 hour respectively.

Next follows a description of the pathological histology of the different organs—liver kidneys adrenals, spleen lungs heart and central nervous system. After this come the various determinations included in the title of the article.

First, the coagulating and anti-coagulating activity of the venom, using a modification of the CERARI and BOUQUET technique which is described minutely. The outcome of the experiments is that 0.001 mgm. produces complete coagulation of 2 cc. of citrated plasma in 15 minutes. With a dose of 5–10 mgm. anti-coagulative action is revealed, or less if the time of action is prolonged.

The authors next prepared the following substances: (1) Fibrinogen from citrated horse-plasma. (2) Seroxyme by SAMSON WRIGHT'S method. (3) Cytoxyme from Lederle's thromboplastin and (4) Thrombin by adding to blood serum 15 volumes of alcohol, collecting the precipitate after several weeks washing it with alcohol and drying it in a desiccator. It is used as an emulsion in saline. With these, eleven series of experiments (excluding control tests) were carried out adding the venom in doses ranging from 0.000,005 to 25.0 mgm. to these substances, singly or in combination and noting the results as regards coagulation. These are given in a table, or rather a series of tablets and discussed. The following conclusions are drawn—

1. The coagulant action of *Echis carinatus* venom on fibrinogen is in part, due to a pseudothrombin.
2. Cytoxyme does not sensibly affect this.
3. Seroxyme increases the action and still more when cytoxyme or calcium or both are added.
4. Thrombin increases the coagulant action in the same degree as the last named combination.
5. The venom in somewhat greater dosage has an anti-coagulant action due to proteolytic effects on fibrin or fibrinogen.
6. This anti-coagulant action is inhibited in slight degree by cytoxyme and calcium, in greater degree by seroxyme whether the other two are present or not.
7. Thrombin weakens the anti-coagulant potency to a degree equivalent to that of adding seroxyme.

The authors next proceed to determine the haemolytic action of the venom using normal horse serum heated to 56°C for half-an hour four dilutions of the venom 1 1000 1 10 000 1 100 000 and 1 1 000,000 are added to a 5 per cent. suspension of washed red corpuscles of the horse. The venom of *Echis carinatus* is less potent in this respect than that of *V. aspis* *Crotalus cornutus* or *Naja tripudians* but equal to or even greater than that of the South American snakes *Sepedon haemachates* *Bothrops atrox* and *B. nasuta*.

Other experiments were carried out to determine the proteolytic potency of the venom using fibrin gelatin solidified egg albumin and solidified serum of the horse. Also the hyperimmunization of horses with anavenin and determination of the anti-coagulant the anti-haemolytic the precipitating and the anti haemorrhagic potencies of the serum so obtained.

Taking these many actions into consideration the authors conclude that since the venom of *Echis carinatus* contains so many constituents—cytolytic haemorrhagic neurotoxic haemolytic necrosing liquefactive and coagulant—the determination of the antitoxic power *in vivo* remains the only way of measuring the true protective value of an antivenene. H Harold Scott

ROY A. C. Leethin and Venom Haemolysis [Correspondence.] *Nature* 1946 June 9 696-7

KLEINMAN A. PAGE R. C. & PREISLER, P. W. Prothrombin Studies using Russell's Viper Venom. VII Effect of Prothrombin Clotting Time of the Concentrations of Calcium and other Salts. *J Lab & Clin Med* 1945 May v 30 No 5 443-50

GRASSET E. Anavenoms and their Use in the Preparation of Antivenomous Sera. Polyvalent Anti *Bitis arietans* *Naja flava* Serum and Specific Antivenenes against African Viperine and Colubrine Venoms. *Trans Roy Soc Trop Med & Hyg* 1945 July v 38 No 6 463-88 [15 refs.]

The author and his fellow workers have shown on previous occasions the value of anavenoms—a term proposed by RAMON in 1925 for venoms detoxicated by addition of formal—in obtaining in a comparatively short period highly potent antivenenes. The method has been in use for more than a decade at the South African Institute for Medical Research.

Several factors have to be taken into account in producing anavenoms, such as the venom concentration the solvent the concentration of formal the pH and buffer the temperature and the period of detoxication. In the present paper an account is given of the details of the procedure and technique. First is considered the question of the concentration of venom to be used in detoxication and the amount of formal sufficient to detoxicate while interfering as little as possible with its antigenic properties. This was done with *Bitis arietans* (the common puff adder of South Africa) *B. caudatus* *B. cornutus* *B. gabonica* and *B. nasicornis* *Causus rhombatus* *Naja flava* and *Sepedon haemachates* and others and at the Institute there has been prepared a polyvalent antivenene against the African snakes of the *Naja* *Sepedon* and *Bitis* genera. The details are of much interest and are so clearly set out that any worker in this field can follow and repeat the instructions. Interested workers must consult the original to reproduce them here would occupy too much space.

The author next considers the rôle of buffer and the pH in anavenom preparation showing that the main effect is on the physical condition of the product. For obtaining antivenenes horses are injected with mixed anavenoms in graded dosage a week after the last injection a sample of the blood is taken

for an *in vitro* test of the titre and if this is satisfactory the horse is bled (10 litres) and, two days later another 10 litres are removed. After 4-6 weeks rest the animals are re-immunized by three subcutaneous injections of the anavenoms at weekly intervals and, as before, the serum is tested and a week later the horses are again bled. When the response begins to fall off and supplementary injections do not restore it, the animal is discarded. [See also this *Bulletin* 1934 v 31 103 1936 v 33 382, 383 1937 v 34 722 723 1939 v 35 522 1940 v 37 514]

H. Harold Scott.

ARUJA, M. L. & BROOKS, A. G. *In vitro* Test for Assay of Potency of Cobra Antivenens. *Indian J. Med. Res.* 1944 Oct. v 32, No. 2 227-31

Snake venoms having a complex antigenic structure there is no international standard of the potency of antivenenes. The results of tests on pigeons *in vitro* are very varied even with birds of the same weight and with the same venoms and antivenenes so that to obtain an average many pigeons may have to be sacrificed. Hence the need for a better and more reliable method.

The observation has been made that washed red corpuscles of certain animals the guinea-pig, for example, are haemolysed by cobra and daboia venoms but that this haemolysis is inhibited if antivenene is present. The authors have therefore devised an *in vitro* method of estimating the antihaemolytic titre of cobra antivenene and this was found to be so closely approximate to the antineurotoxic titre in pigeons that it is suggested as a substitute for the latter. The procedure is on standard lines. The haemolytic effect on guinea-pig cells is estimated by adding diluted venom in graded doses to 3 per cent. suspension of the cells. Then another series is set up in which the venom and the serum under test, made up to a fixed amount, are shaken and then incubated at 37°C. for an hour after which a fixed quantity of the red cells in normal saline is added, the whole shaken to procure good mixing, and allowed to stand at room temperature for 18 hours, when the result regarding haemolysis is noted. An example is given in these words—

"The sample of venom used in the *in vitro* test had a minimum haemolytic dose of 0.03 mg. for 1 cc. of 3 per cent. guinea-pig cells, and that used for the *in vivo* test had a minimum lethal dose of from 0.3 mg. to 0.4 mg. for pigeons of standard weight. The anti-haemolytic potency of the various sera tested varied and according to the results obtained they have been arranged in three different categories. In group A haemolysis—partial or complete—occurs with 0.4 mg. or less of venom. In group C partial or no haemolysis occurs with 0.6 mg. of venom, and in the intermediate group B partial or complete haemolysis occurs with 0.5 mg.

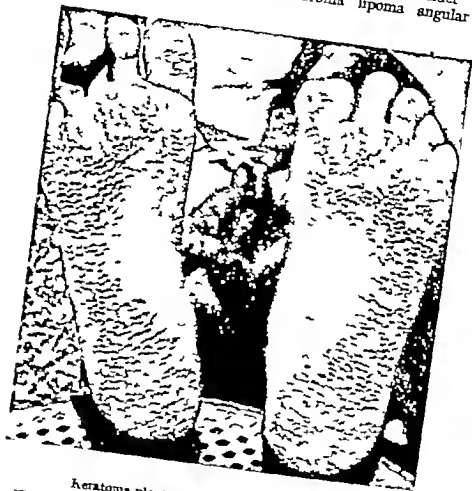
The close correlation between the *in vitro* haemolysis and the *in vivo* tests with pigeons is shown by the fact that group B serum, in which 0.4-0.5 mgm. of venom is neutralized by 1 cc. of the antivenene may or may not pass the *in vitro* test, but group C serum (0.5 mgm. venom being neutralized) does pass the test. Hence it is concluded as generally true—there are occasional anomalies—that "if the anti-haemolytic titre of a serum is less than 0.4 mgm. per cc. it is not up to standard titre; if it is over 0.5 mg. per cc. it is up to titre and if it is between 0.4 mg. and 0.5 mg. per cc. it is on the border line and may or may not be up to titre."

H. Harold Scott.

DERMATOLOGY AND FUNGOUS DISEASES

FASAL, P. Cutaneous Diseases in the Tropics a Clinical Study based on Observations in Malaya *Arch Dermat & Syph* 1945 Mar v 51 No 3 163-71 7 figs.

This is entitled a clinical study, but is little more than a list of cutaneous conditions met with during three years in Malaya. More than 70 diseases receive mention in these few pages. The author includes under cutaneous diseases such things as new growths fibroma lipoma angular stomatitis



Keratoma plantare sulcatum on a Tamil man.

[Reproduced from the *Archives of Dermatology and Syphilology*.]

from irritating fruits also the rash of dengue tsutsugamushi fever lympho-granuloma inguinale Madura foot elephantiasis and others.

The author divides the diseases into three large groups (1) Those due to external causes among which he mentions sunburn sudaminal rashes prickly heat dhobie itch and various forms of dermatitis venenata as rengas and upas tree (*Anilaris toxicaria*) rashes necrosis from injuries inflicted by catfish and the sting ray scorpion stings etc. cheilitis from mango papaya and other fruits Also keratoma plantare sulcatum probably due to walking barefoot on hot and moist soil. A good example of this is shown in a photograph (2) A second group comprises conditions associated with nutritional deficiencies such as ichthyosis crazy pavement skin pellagra and angular stomatitis (3) Thirdly cases

arising from infection by animal and plant organisms. Among these the author places the exanthemata—dengue, varicella herpes zoster molluscum contagiosum, Japanese River fever venereal diseases also impetigo and furunculosis, tuberculosis and leprosy, pityriasis versicolor eczema marginatum and tinea umbricata, tropical ulcer and elephantiasis. Lastly mention is made of urticaria purpura, erythema occurring in malaria patients taking quinine, also of psoriasis and lichen planus. These all receive passing mention but rarely more than a few words each. Obviously hardly more could be said when so many conditions are referred to in so small a space. *H Harold Scott*

FERNÁNDEZ, J. M. M., VACCARO A. SERIAL, A. & CARBONI E. Discromias de probable etiología espiroquetónica (Mal de Pinto ?) [Dyschromia associated with Spirochaetosis, Pinto ?] *Rev Argentina Dermatofisiología* 1945 Mar v 29 No 1 1-10 6 figs.

Notes are given of five cases of a peculiar symmetrically distributed achromia in patients whose ages ranged between 10 and 54 years. Face trunk and limbs were affected. The Wassermann reaction was negative (except in one



Case of symmetrically distributed achromia.

[Reproduced from the *Revista Argentina de Dermatofisiología*]

where it was doubtful and the patient gave a history of contracting syphilis years before) Spirochaetes were to be seen in fluid obtained at the edge of the patches. The authors are of opinion that the condition is not something new but merely a variety of mal del pinto. *H Harold Scott*

ONKERMAYER, M. E. & FROST K. Some Phases of Vitamin Therapy in Dermatology *Arch. Dermat. & Syph.* 1945 May v 51 No 5 300-12. [21 refs.]

The authors would divide a varied group of dermatological conditions into two groups—(a) in which an aetiological relationship has been established

between the condition and a specific vitamin and (b) dermatoses in which a true vitamin deficiency is either debatable or undemonstrable but for which vitamin therapy appears to be of benefit.

They appear to agree with the observations of others that a high intake of vitamins A C D and the B complex aid in the control of the allergic state or the allergic factor in a variety of dermatological conditions their action possibly being due to the antidermatitis and hypochlorhydria preventing fractions of the B complex. It is suggested as a warranted fact that the ingestion of thiamin will render a sensitive subject tolerant to insect bites or even repellent to the insects themselves.

In regard to vitamin A it is stated large doses seem to affect a large number of dermatological diseases by their influence on the integrity and resistance of epidermal and epithelial surfaces but the mechanism of the effect of vitamin A on the epithelial tissues has not been explained the skin contains no vitamin A and carotenoid levels of the blood plasma of patients with a number of diverse cutaneous diseases have not revealed characteristic deviations.

Attention is focussed on those dermatoses characterized by excessive keratinization either more or less diffuse or limited to the follicular system. Abnormal callus formation of the skin and hyperkeratotic chronic simple lichen are stated to respond, and among the second group lichen pilaris keratosis follicularis pityriasis rubra pilaris and acne vulgaris are represented as having been cured.

These conditions are quite apart from the follicular hyperkeratosis which the authors admit as many others have done as a specific sign of vitamin A deficiency.

[Doubtless vitamins play a part in maintaining the nutrition of the skin but when it is necessary to give from 20 to 100 times the normal daily intake over a period of 6 to 18 months to effect a change in the above-mentioned conditions one begins to wonder whether any effect produced is of the nature of a specific response to such treatment. Recently doubt has been cast upon the belief that follicular hyperkeratosis is a sign of vitamin A deficiency. The wise man will continue to experiment but reserve his interpretation of results till later.]

SYMMERS D. Experimental Reproduction of Maduromycotic Lesions in Rabbits
Arch Pathology 1945 June v 39 No 6 358-63 5 figs
H S Stannus

Phialophora jeanselmei when injected subcutaneously into rabbits produces solitary non-ulcerative nodules which histologically are specific and are closely comparable to the nodules in that form of maduromycosis in man which is caused by the same fungus.

EMMONS C. W. *Phialophora jeanselmei* comb. n. from Mycetomas of the Hand. *Arch Pathology* 1945 June v 39 No 6 364-8 2 figs [12 refs.]
The mycologic characteristics of a fungus isolated from mycetoma of the hand are given. The condition developed after an injury in which splinters from a wooden floor pierced the skin. The fungus resembles *Phialophora* which is known to occur on wood. It is specifically identified with *Torula jeanselmei* Langeron which was isolated from mycetoma of the foot. This species is transferred to *Phialophora*, the name becoming *Phialophora jeanselmei* comb. n.

LEVY B & BLACK SCHAFFER, B. Studies in Experimental Systemic Mycosis. I. Systemic Chromomycosis (Chromoblastomycosis) in Mice Preliminary Study. *Amer J Trop Med* 1945 Mar v 25 No 2, 117-27 11 figs.
The lesion of chromomycosis is cutaneous-subcutaneous and metastatic spread of the infection to the deeper tissues is so rare that only two instances (41)

are recorded in the literature. To investigate the possibility of infection of the deeper tissues, Levy and Black Schaffer inoculated five white mice by the intravenous route and five others by the intraperitoneal route with a fresh culture of the causative fungus *Horodendron pedrosoi* ground up and suspended in isotonic saline. The mice were sacrificed and examined at intervals between the 7th and 27th days following inoculation. Intraperitoneal inoculation caused only a local lesion with, in one case slight extension of the infection into the stomach wall. Intravenous inoculation, as would be expected, led to widespread distribution of the fungal elements with milium granulomatous lesions mainly in the lungs—the first capillary area encountered—and in lesser degree in the kidneys. The cytological structure of the granulomata was of the kind associated with chromomycoses and other mycoses and was not merely a foreign body reaction. In many of the granulomata there was evidence of survival and growth of the fungus and in one case, small satellite lesions suggested an extension of the infection. The time allowed for survival of the mice after inoculation was too short to determine that a progressive infection had been established. The experiments will therefore be repeated with longer time intervals.

J. T. Duncan

RODINUX J. Documents complementaires au sujet des teignes au Mayumbe. [Additional Information on the Ringworms of Mayumbe.] *A n Soc Belge de Med Trop* 1943 Sept-Dec 23 Nov 3-4 237-8 8 figs on 2 pls

TROPICAL ULCER.

WALKER TAYLOR, F. N. Treatment of Tropical Ulcer. *Lancet*. 1945 July 14 40-42.

"Tropical ulcer is a straightforward subject and difficulties are created only by a wrong conception of its nature.

"The treatment is elementary. This is attained by two rational steps. (1) Arranging conditions so that fresh granulations will fill the tissue gap. (2) Arranging conditions for re-epithelialisation of the surface before fibrosis has been allowed to develop.

The author points out that the above refers to the treatment of the "de novo" tropical ulcer as it is first seen.

(1) The first step is taken by insisting on continuous stay in bed, and for West African natives the leg must be tied to a fixed appliance to keep the patient in bed. This is all that need be done but warm moist compresses and penicillin or sulphonamide powder locally are useful aids and, since dressings must not be allowed to become dry, soft paraffin is the best application.

(2) The ulcer being now clean and filled with granulations skin grafting should be done without delay. The author prefers "pinch grafts."

When a toenail is involved, sufficient drainage must be provided by cutting away dead cuticle and dead nail. Then the cavity is disinfected and packed with gauze soaked with 10 per cent silver nitrate solution, to prevent pus from passing into it from the surrounding part of the ulcer.

The author gives two tables for comparison. The first analyses 210 cases of tropical ulcer admitted to hospital and treated in various ways from January 1st to May 31st, 1944 and the second analyses 47 cases admitted to the author's wards from July 10th to October 10th and treated in the way described above. In the latter group the average time of healing (17.8 days) was less than half that (37.2 days) in the former.

In a letter to the *Lancet* 1945 July 28 124 MILLS points out that acute ulcers spread very rapidly and that the application of pure carbolic is the best means of preventing this and of securing a granulating surface for pinch grafts.
J F Corson.

SORICELLI, F. Contributo radiologico alla conoscenza di alcune lesioni osteo-periosteae nell'ulcera tropicale. [Radiological Investigation of Osteo-periostitis in Tropical Ulcer] *Boll Soc Ital di Med e Igien Trop* (Sex Entrea) 1944 v 4 No 3 487-96 English summary (6 lines)

MISCELLANEOUS DISEASES.

BINNS R. T. A Study of Diseases in Australian Natives in the Northern Territory
Med J Australia 1945 Apr 28 v 1 No 17 421-6.

These observations were made during the occupation of the Northern Territory of Australia by the army. A native hospital was built near the Australian general hospital and was situated on the bank of the Katherine River [apparently about 14 30 S. x 132° E]. Patients came from all parts of the northern districts of the territory and various surrounding settlements were visited and medically surveyed. From September 1943 to October 1944 about 400 natives were treated at the hospital and about 250 were examined at the settlements. Surgical cases and ophthalmic cases are not included in this report but the author mentions that a large majority of natives were found to be suffering from trachoma.

The diseases which affected natives more than white people were yaws, ankylostomiasis, granuloma venereum [ulcerating granuloma of the pudenda] and leprosy. The Kline test of the blood was positive in 193 (48 per cent.) and 81 had clinical signs of yaws. Hookworm ova were found in 12 per cent of natives admitted to hospital usually the infestation produced no symptoms but in a few cases severe anaemia was caused. There were 20 cases—10 in each sex—of granuloma venereum and 12 cases of leprosy.

The diseases common to both natives and white people included pneumonia (32), pulmonary tuberculosis (21), acute rheumatism (5), meningitis (1), mumps (24), benign tertian malaria (20), Flexner type of dysentery (4), amoebic dysentery (2) and gonorrhoea (11). The course of tuberculosis in natives was similar to that in Europeans and the frequency of the occurrence of fibrosis and calcification indicated the existence of some natural resistance. The authors think that the problem of control is not so hopeless as has sometimes been taught.
J F Corson.

DUBOIS A. La pathologie du Congolais. [Diseases of the Inhabitants of the Belgian Congo.] *Ann Soc. Belge de Méd Trop* 1943 June 30 v 23 No 2, 69-89 [31 refs.] 1944, June 30 & Sept. 30 v 24 Nos. 1-2 & 3 13-28. [54 refs.] 79-100 [61 refs.]

In these papers the author gives a general survey of the prevalence of various pathological conditions among Africans of the Belgian Congo. The account was largely written from memory in the absence of records; some information was received from colleagues. Many references are made to work in other parts of tropical Africa and the Far East.

Chronic valvular disease of the heart is not rare; acute rheumatism being

very rare, the causes are not known but it is thought that syphilis is one. Aneurysm of the aorta and large arteries and endarteritis obliterans are also not rare.

Brunchopneumonia is commoner than lobar pneumonia. Loeffler's syndrome has recently been observed.

Among diseases of very rare occurrence are peptic ulcer, appendicitis and calculus (biliary, renal and vesical). Cirrhosis of the liver apart from schistosomiasis is probably not common but the author has no figures. Gout is common in some places, exophthalmic goitre is unknown.

Haematology has been studied by VAN DEN BERGHE (this *Bulletin* 1943 v 40 282). RODHAIN (personal communication) observed 2 cases of Hodgkin's disease.

Among diseases of the nervous system, epilepsy is fairly common in certain areas. GREGOIRE (unpublished) at Léopoldville noted 24 cases of cerebral syphilis and 8 of general paralysis among 155 insane natives.

Skin diseases were investigated by DUBOIS and BRUYNSZELS (this *Bulletin* 1943 v 40 176).
J. F. Corson.

SUÁREZ R. M. The Incidence of Heart Disease in Puerto Rico. Statistical Analysis of 1,081 Cases. *Amer Heart J* 1945 Mar v 29 No 3 338-47 1 fig. [19 refs.]

All of those with whom this analysis deals were native Porto Ricans, their ages ranged between 8 and 83 years, only 10 per cent. were negroes, one-third were females, two-thirds males. Examinations were thorough with electrocardiograms, cardiac measurements, vital capacity, venous pressures, and the Wassermann, Kahn or Kline tests. In the 27 years since 1918 heart disease as a cause of death had risen from seventh to fourth place, being surpassed only by intestinal conditions, tuberculosis and pneumonia. Among 1,259 consecutive autopsies 128 (10 per cent.) were found to have cardiovascular disease as the cause of death, and of these 33 (30 per cent.) were syphilitic, 26 (20 per cent.) rheumatic and 22 (17 per cent.) arteriosclerotic. Just over half the syphilitics (20 of the 38) showed aortic aneurysm.

In 1942 heart disease was the cause of death of 2,177 or 111.9 per 100,000 population, the urban rate being more than double that of the rural (170.2 to 81). Rheumatic fever is generally believed to be rare in the tropics, this applies to joint symptoms and clinical manifestations, but rheumatic heart disease is far from uncommon.

Among the 1,081 analysed there were 18 per cent. (163) cases of coronary disease and 40 per cent. of those with arteriosclerotic heart disease presented evidence of myocardial infarction.

In Porto Rico the percentage incidence of the chief types of heart disease is: arteriosclerosis 30.9, hypertension 22.8, rheumatic fever 17.4, syphilis 8.1. The author compares these Porto Rico figures with those of Mexico, Virginia and Louisiana in a table from which it is seen that Porto Rico is highest in arteriosclerosis, but lowest in syphilis.
H. Harold Scott

APLEY J. & GRANT G. H. Tropical Eosinophilia as seen in England. *Lancet*, 1945 June 30 812-13 [19 refs.]

In September 1944 the authors reported on a case of tropical eosinophilia in an Englishman home from India. They drew up a very useful table contrasting the so-called Loeffler's syndrome with typical "tropical eosinophilia" and then demonstrated that none of the differences thus set down was really valid, but represented extremes of one condition (this *Bulletin* 1944 v 41 1063).

The authors now record four more cases three very similar to the first the fourth showing certain differences among 113 consecutive patients invalided home from the East on account of pulmonary conditions chiefly asthmatic. A table summarizes the chief features of all five cases (the original and the four new ones) showing that four of the patients had been in India [the cases are oftenest reported from the Bengal coast] and one in China after a brief stay in Ceylon all complained of cough bronchitic or asthmatic symptoms worse at night with loss of weight. Eosinophilia ranged between 7 and 32 per cent. before treatment with arsenicals in England reduced to 1-5 per cent two weeks after a course of NAB.

In view of the various conditions which have been assigned [largely on account of their concomitant presence] as causes of the syndrome numerous investigations were carried out on all five patients notably repeated X ray examinations of the chest blood counts faecal examinations for helminths or their ova sputa and blood for filariasis.

Treatment consisted of arsenic injections three intravenously of 0.3 gm. of neosarsphenamine followed by three more of 0.45 gm. also intravenously with ascorbic acid and calcium gluconate at 3-4 day intervals. During the course the eosinophilia increases but it falls within a fortnight afterwards either rapidly or more slowly over a period of several weeks.

The authors conclude that these are allergic manifestations the common result of perhaps several kinds of allergen introduced it may be by mites where such have been found (as by CARTER *et al* this *Bulletin* 1945 v 42 73). The fifth case differed from the others notably in the characters of the cells seen in smears from sternal puncture and the authors think that this patient was not suffering from the same disease as the others [or it may be that the allergen was not the same]. A remarkable difference from the cases generally recorded is the absence of splenomegaly from all five [Nothing is said of any lymph gland enlargement as reported by VAN DER SAR and HARTZ (below) and others. The more this condition is studied the more complicated it becomes and the difficulties instead of being cleared up seem to increase. There is here an excellent field for research.]

H Harold Scott

VAN DER SAR A & HARTZ H The Syndrome Tropical Eosinophilia and *Microfilaria*. *Amer J Trop Med* 1945 Mar v 25 No 2 83-96 8 figs. [25 refs.]

The author starts his paper with a good survey of the literature of the last quarter of a century dealing with Loeffler's syndrome eosinophil lung tropical eosinophilia. He then relates four cases three of them under his own observation with leucocytosis eosinophilia (relative and absolute) nocturnal asthma with splenomegaly and enlarged lymph glands. The fourth case was that of a boy of 7 years killed in a motor accident in life he had recently suffered from asthma and anaemia. In the first three improvement and final recovery followed the administration of arsenicals.

The important point of this contribution is that sections of the glands in the first and of the spleen in the last case showed the presence of microfilariae with local eosinophilia (eosinophilic abscesses). In the other two the pathological histology was similar but no worms were seen (but in one at least serial sections were not made). The only known *Filaria* in Curaçao is *W bancrofti*.

The authors maintain therefore that there seems to be a relationship between filariasis and tropical eosinophilia but whether all cases of this syndrome are so related can only be determined after many more have been

examined, by biopsy of enlarged glands for example, in the various places where these cases have been reported. Photomicrographs showing the pathological histology are well reproduced.

H Harold Scott

HIRST W R & McCANN W J Tropical Eosinophilia Report of a Case. *U.S. Nat. Med. Bull.* 1945 June v 44 No 6 1277-81 1 fig

The main interest of this case lies in the fact that the patient, though he had served in the South Pacific and other warm climates had never been in India. His symptoms were typical feverishness malaise headache asthmatic attacks, especially at night, with leucocytosis to about twice normal and an eosinophilia to 82 per cent. His symptoms had begun two years prior to his coming under the author's care when he was in Samoa. None of the ordinary causes of eosinophilia was present (except the asthma) there were no indications of helminthic infestation the Kahn reaction was negative. He was given neosarsphenamine starting with 0.15 gm. then at four-day intervals 0.3 0.45 0.6 and 0.6 gm. The response was dramatic. At first there was a fall of leucocytes, followed, as usual, by a rise, though of the eosinophiles to a less degree, and then a reduction of the total leucocytes and of the eosinophile percentage. In three weeks the total had dropped to normal, but the eosinophiles were still 20-25 per cent. later they fell to 4-16 per cent. and the patient never felt better.

Among the authors' conclusions are (1) That, since the symptoms had recurred all the usual forms of treatment for almost two years they might very likely have persisted indefinitely had not the specific treatment with arsenic been started. (2) That the ready response to arsenic points to a spirochaete or a protozoan as the cause. (3) That either the disease is endemic in the South Pacific, or infection is transmissible from man to man, for the patient had been in contact with East Indians at Panama, though he had never himself, as already stated, been in India.

H Harold Scott

CHAUDHURI, R. N. & RAI CHAUDHURI, M. N. A Case of Tropical Eosinophilia developing Agranulocytic Angina during Arsenical Therapy *Indian Med. Gaz.* 1945 Mar v 80 No 3 151-3 1 pl & 1 chart

GENERAL PROTOZOOLOGY

KIRBY H. Some Observations on Cytology and Morphogenesis in Flagellate Protozoa. *J. Morphology* 1944 Nov., v 75 No. 3 361-421 1 text fig & 8 pls. (67 figs.). [165 refs.]

Certain flagellates apart from the evident external structures such as flagella and undulating membranes possess complicated internal structures or organelles of which the blepharoplasts kinetoplasts, parabasals, costa and axostyles are examples. When multiplication by binary fission occurs some of these divide, one product passing to each daughter individual others are completely absorbed, new organelles being developed for each daughter flagellate. In the paper considered here the author discusses the behaviour of a number of flagellates in these respects making special reference to some of the larger forms found in termites, certain trichomonads and *Trypanosoma brucei*. The paper which is well illustrated, should be read by those interested in the morphology of the group of Protozoa.

C M Wenyon.

MANWELL R. D COULSTON F BLACKLEY Ellen C. & JONES Virginia F
Mammalian and Avian *Toxoplasma* J Infect Dis 1945 Jan.-Feb
v 76 No 1 1-14 8 figs on 1 pl. [20 refs]

This is an interesting review of knowledge regarding three types of parasite which have been referred to as toxoplasma combined with an account of certain original observations and experiments. In the first place a study was made of a mammalian strain of human origin. This was inoculated to four species of mammals and six species of birds. Attempts to infect frogs failed entirely. Infections were produced by intracerebral and intraperitoneal inoculations as well as by feeding on infected tissues. It would seem that all warm blooded animals are susceptible there being amongst them a complete lack of host specificity. The type of infection varied being sometimes acute and at other times chronic. After intracerebral inoculation the infection and symptoms were chiefly cerebral, while after intraperitoneal inoculation they were mostly abdominal though in both cases generalized infection occurred in which different organs and many types of cell became involved. As regards the natural method of transmission there is little information. Healthy animals failed to become infected when kept in contact with those infected though intestinal washings or infected animals produced infection by the mouth. Infected mice pass the infection to offspring *in utero*. The parasite is easily killed by drying and disinfectants. It will survive in the ice box for not longer than 48 hours but will withstand complete freezing for a short time. The only method of cultivation which was successful was the chick-embryo method within the egg.

The second type of toxoplasma has been found in small birds where it is commonly seen in lymphocytes lying in a notch in the nucleus. It is completely host-specific all attempts to subinoculate having failed. Birds infected with it are in no way protected against the mammalian toxoplasma. Furthermore it can be distinguished morphologically. The authors conjecture that it is not a toxoplasma but probably represents straying merozoites of a coccidium. The third toxoplasma the λ bodies is also of avian origin and is found commonly in the lungs of canaries and possibly other small birds. Like the second it is not inoculable to other hosts and fails to give protection against the mammalian form. It also may represent merozoites of a coccidium.

The general result of the enquiry is that the mammalian form alone belongs to the genus *Toxoplasma* and that all strains isolated from mammals will be found to belong to the original species *T. gondii* of NICOLLE and MANCEAUX though various authors have given specific names according to the hosts in which the parasite has been found.

C M Wenyon

GENERAL ENTOMOLOGY

BUYTON P A. The Use of the New Insecticide DDT in relation to the Problem of Tropical Medicine Trans Roy Soc Trop Med & Hyg 1945 Mu
v 38 No 5 367-93 [32 refs] Discussion 393-400 [SCOTT H (President) MACDONALD G BUSVINE J R. MELLANBY K SINTON J A WENYON C M BUYTON P A (in reply)]

The ideal insecticide in addition to being highly toxic to insects should be safe to man and mammals and stable under natural conditions. It should not stain, have an offensive smell or harmful effect on fabrics, metals etc. It should be easily manufactured at low cost and be adaptable to many methods or purposes. DDT, dichlor-diphenyl trichlorethane or alpha alpha-bis

(p-chlorophenyl) beta beta beta trichlorethane fulfils these requirements more nearly than any other substance. It is an exceedingly non-volatile white crystalline powder with a faint pleasant smell. It melts at 108°C. the molecular weight is 354.5 the density 1.6 grammes per ml. and it dissolves in most organic solvents, though the solubility in water is very low. In mineral oils it tends to be more soluble in the less highly refined specimens, the solubility in kerosene being 4 per cent. that in various fuel oils 8 to 10 per cent. Commercial samples are usually mixed with other substances mostly isomers which are only slightly insecticidal, and have a purity of 60 to 70 per cent.

Solid DDT ground with a mineral diluent is harmless when applied to the skin, and does not retard the healing of cuts. When applied to the skin in solution DDT is absorbed and symptoms occur in experimental animals after daily application of 150-1,200 mgm. per kgm. Dimethyl and dibutyl phthalates do not increase the absorption of DDT in comparison with other solvents. There are no records of dermatitis after DDT and sensitization is uncommon. It is not harmful to the eye including the conjunctiva, and ointments up to 5 per cent. have been put on the conjunctiva without ill-effect.

When experimental animals and men are exposed to concentrated mists of DDT solution, and dusts of the powder they do not suffer ill effects and no danger is to be expected following inhalation of sprays or dust during insecticidal work. However precautions should be taken to prevent the heavy contamination of food.

When single doses of oil solutions are given to experimental animals by the mouth, the median lethal dose varies from 150 to 600 mgm. per kgm. and continuous dosage with 50 mgm. per kgm. per day is fatal to rabbits. Symptoms are slow in onset, initiated by abnormal excitability and tremors going on to flaccid paralysis and death. [For an account of symptoms in man see WIGGLESWORTH, *Bulletin of Hygiene* 1945 v. 20 411] At post-mortem examination in animals exposed to toxic doses of DDT minor nervous changes are seen with large areas of necrosis in the liver. The author concludes that DDT used as an insecticide is quite safe.

DDT is more general and less specific in its action on arthropods than most insecticides but the lethal dose for different insects varies greatly that for *Rhodnius* for instance being 10,000 times that for *Aedes*. It acts as a contact poison and has a very slow effect death being preceded by unco-ordinated and violent movements. It is not repellent to insects and is not a fungicide.

Against flies and mosquitoes it may be used as a spray most such sprays now consisting of DDT to kill the insect with some pyrethrum to ensure quick knockdown or as a film on surfaces. Films for which a dose of 100 mgm. per sq. ft. should be aimed at hold the number of mosquitoes in treated rooms down to a very low figure for 2 or 3 months after a single application. Much entomological work is necessary on this subject as the probability of killing is influenced by the habits of the mosquito and the type of place in which it rests. A particularly important point is that the use of such films may solve the problem of transport of insects by aircraft. Field tests of the dry powder as a larvicide have been disappointing despite encouraging laboratory results, but 5 per cent. oil solutions have proved effective in doses of 1 to 2 quarts per acre and under experimental conditions in doses as low as 0.1 cc. per square yard (0.85 pints per acre) which gives some residual effect needing further enquiry as does the use of colloidal solutions. Distribution of oil solutions by aircraft not only kills larvae but also many adult mosquitoes contaminated either directly or by picking up DDT from surfaces at night.

Adult house flies may also be killed by sprays or films the recommended strength of sprays being 0.3 or 0.5 per cent. with 0.05 or 0.03 per cent. pyrethrins respectively. Films of 25 mgm. per square foot are effective though the

dose varies with the nature of the wall surface painted surfaces needing more than plain wood and glass surfaces very minute quantities It has also been shown that many other muscids including *Calliphora* *Lucilia* *Chrysomya* *Stomoxys* and *Glossina* are very susceptible to DDT in the form of a residual film and very promising results in their control have been obtained DDT has also been used in emulsion against the larvae of the housefly with success

As an insecticide against lice DDT is very valuable and a 10 per cent. mixture with talc is now commonly used it remains effective for 2 or 3 weeks and may kill lice after that assuming that the subject does not wash his garments. For men in winter clothes $1\frac{1}{2}$ ounces per treatment suffices It was used in the control of typhus in Naples early in 1944 on a very large scale and this has been described as the only completely proven victory which can as yet be ascribed on DDT's battle honours An even more effective method is by impregnating garments with 1 to 2 per cent of DDT from solutions or emulsions.

DDT has also been used against head lice as a dust or in emulsions in which form 0.2 gm. completely proofs the head for a week

DDT is without doubt the most effective material known for bug control. Experimentally films of about 0.2 mgm. per square cm (180 mgm. per square foot) remained lethal for from one to six months The type of surface and the method of application affect results and dosage In practical trials it has been found that a dose of about 100 mgm per square foot kills any bugs brought in within three months

Cockroaches are relatively resistant to DDT A five per cent powder is very effective against fleas. Trombiculid mites die after running on impregnated garments but as the effect is slow and wears out with washing this method is of little value against the vector of scrub typhus There has been recorded however a marked reduction in mites on ground dusted with 30 lb of 2 per cent DDT per acre

[The author refers to the non-appearance so far of any accurate account of the use of DDT in the Naples typhus epidemic of 1943-44 A statement giving the weekly incidence of cases the dates on which DDT was used and the scale on which it was used must be awaited before DDT can be given credit for ending the epidemic]
G Macdonald

- (i) ROARK R. C. A List of Publications on 2, 2-bis (Parachlorophenyl)-1, 1-Trichloroethane (called DDT) from 1874 to April 30 1944, Inclusive U.S. Bureau Entom & Plant Quarantine 1944 June 12 pp [Processed.]
- (ii) — & McINDOO N. E. A Digest of the Literature on DDT through April 30 1944 U.S. Bureau Entom & Plant Quarantine 1944 Dec. E-631 53 pp [Processed.]
- (iii) — A Second List of Publications on DDT U.S. Bureau Entom & Plant Quarantine 1945 May E-660 27 pp [Processed]
[Summary appears also in *Bulletin of Hygiene*]

In June 1944 the U.S. Bureau of Entomology and Plant Quarantine issued a list compiled by ROARK of 174 articles on DDT published from the time of its original synthesis in 1874 up to April 30 1944 In December 1944 a digest (E-631) by ROARK and McINDOO of these 174 articles was published. Much of the information abstracted relates to tests of DDT insecticides against plant pests under laboratory and small field plot conditions but among records of DDT tests against 132 identified species of insects and other arthropods there are notes relating to cockroaches lice bedbugs, house and stable flies ticks and harvest-mites of possible medical or hygiene interest A second list of publications on DDT designed to bring the bibliography of this subject up to date and also to call attention to a few older publications that were overlooked

at the time of compiling the first list appeared in May 1945 (E-660). This second list by ROARK includes a further 418 titles published up to December 31 1944
R L Sheppard

HALL S. A. SCHRECHTER, M. S. & FLECK E. E. Chemical Determination of DDT
U. S. Bureau Entom. & Plant Quarantine 1944 Nov ET-211 6 pp
1 fig. [Processed] [Summary appears also in *Bulletin of Hygiene*]

A modification of Winter's method for the determination of halogen in organic compounds (*Indust. & Engin. Chem. Analyst. Ed.* 1943 v 15 571-4) has been adapted to the determination of DDT. About 1 hour is required for an analysis to be carried out and the method is sufficiently sensitive for the determination of DDT in spray residues
R L. Sheppard

LAFFIT Marguerite & NICOLLE, P. Recherches sur la nutrition des réticulés hémaphages. IV. Alimentation de *Trypanosoma infestans* Kling a l'aide de sérum de cheval. Action du glucose. [The Feeding of *T. infestans* with Horse Serum. Action of Glucose.] *Bull. Soc. Path. Exot.* 1944 v 37 Nos 1-2, 38-51 7 figs.

CHING HUA MENG & WOODFIELD G. F. Studies on the Control of Faecal-borne Diseases in North China. XVIII. An Approach to the Quantitative Study of the House-Frequenting Fly Population. E. The Food Preferences of the Common North China Fly. *Chinese Med. J.* (Chengtu Edition) 1943 v 61A, 102-3 [10 refs.] F. A Preliminary Study of the Life Histories of *Musca vicina* Macquart and *Chrysomya megacephala* Fabricius. *Ibid.* 1943 July v 61A, 181-5 [19 refs.]

CHING HUA MENG & WOODFIELD G. F. Studies on the Control of Faecal-borne Diseases in North China. XXVIII-XXXI. Comparative Studies on the House-Frequenting Fly Population of Szechuan, West China. A. The Characteristics of the West China Fly Population. *Chinese Med. J.* (Chengtu Edition) 1943 Oct. v 62A, No 1 8-11 1 fig. B. The Breeding Habits of the Common West China Flies. *Ibid.* 1944 Jan v 62A No 2 71-7 C. Natural Enemies of the Common West China Flies. *Ibid.* 1944 Apr v 62A, No 3 89-92 1 fig. D. Life History of *Sarcophaga fuscicornis* Böttcher. *Ibid.* 1944 July v 62A, No 4 144-9

TURNER, R. G. Human Creeping Myiasis. Report of a Case. *Brit. Med. J.* 1945 July 7 11-12.

This is an account of a case of myiasis caused by the larva of *Hypoderma bovis*. The patient was a boy aged 14 years who lived in London and had never been abroad, but he often went to Epsom Downs. He was admitted to University College Hospital, London on January 21 1944 with the following history of his illness. In January 1943 he felt pricking pains over his shoulders and chest which occurred about twice a month until July 1943 when they stopped, but he then noticed, for the first time a swelling in the arm, about 3 cm. in diameter painless except that it gave a pricking pain on pressure. It lasted for 2 days, but similar swellings continued to appear in various parts of the body. They were 1-5 cm. in diameter and were raised 0.5-1 cm. above the surface of the surrounding skin. They usually remained for a few days and then disappeared. On December 30 1943 one of these swellings showed a central black spot and, after the application of fomentations it burst on January 2, and a white maggot appeared after syringing.

On admission to hospital he appeared to be in good health and there were no swellings. His blood was normal except that it contained 22,000 leucocytes per cmm. with 44 per cent. of eosinophils. A swelling appeared on January 24

in the left temporal region and spread round the orbit and across the forehead and remained until February 1. Others followed on various parts of the body, on February 6 a first instar larva of *Hypoderma bovis* was obtained from a swelling and 3 more were obtained during February from other parts of the body. After March 1 there were no more swellings and the patient was discharged on March 10. up to February 22 1945 there had been no further signs or symptoms.

Human infestation with *H. bovis* has rarely been reported. the author could only find 5 cases in the literature (HERNIM *Medical Entomology* p 342 Macmillan New York MILLER *J Amer Med Ass* 1910 v 55 1978 SMART *Parasitology* 1939 v 31 130). A case of infestation with *H. lineatum* is reported by STYLE [this *Bulletin* 1924 v 21 786] J F Corson

GOLDMAN L. *Pyodermic Myiasis in Children* Observations with special reference to Tórsalo. *Amer J Dis Children* 1945 May v 69 No 5 280-82 3 figs.

A short note on cutaneous myiasis due to the larva of *Dermatobia hominis* seen by the author at Tórsalo Costa Rica [see this *Bulletin* 1941 v 38 351] photographs of the larva and of *Aedes angustivittatus* one of the carriers of the eggs are shown J F Corson

VAN DEN BERGHE L. & BONE G. Cas de myiase intestinale à *Eristalis* [A Case of Intestinal Myiasis due to *Eristalis*] *Ann Soc Belge de Méd Trop* 1944 June 30 v 24 Nos. 1-2, 69-70 2 figs on 1 pl

LABORATORY PROCEDURES

MEDICAL RESEARCH COUNCIL. The Sterilization, Use and Care of Syringes. By a Committee appointed by the Medical Research Council [WILSON G S Chairman] *M R C War Memorandum No 15* 23 pp 8 figs. [44 refs] 1945 London H.M. Stationery Office. [4d] [Summary appears also in *Bulletin of Hygiene*]

There are many records of infections, some serious caused by therapeutic injections and these are usually attributable to some fault in aseptic technique. The syringe and needle may be infected owing either to the use of an inefficient method of sterilization or to contamination afterwards by fingers from the air or by immersion in contaminated water or saline the injection fluid itself may be contaminated, or the source of infection may be the patient's own skin. This memorandum makes recommendations to guard against all these possibilities but is concerned chiefly with the first. It is pointed out that the only processes which ensure absolute sterility in a syringe are autoclaving or exposure to a temperature of 160°C. in a dry oven. The cement of glass-metal syringes may melt at these temperatures the use of all-glass syringes is therefore advocated. These should be enclosed in tubes the ends of which are tied up with kraft paper or Cellophane and they should preferably be sterilized by dry heat. Boiling is given as an alternative with the warning that it cannot be depended on to destroy spores the addition of sodium carbonate to the water will remedy this fault but the resulting alkalinity of the syringe may affect drugs or biological products to be injected.

Members of the Committee responsible for this Memorandum conducted experiments themselves from which they conclude that there is no suitable

spree, all were enlightened by his great intellect. As for adventure what can one think of more adventurous than to carry out, as he did with his brother a post mortem examination in a death chamber with a howling mob of fanatical and angry Chinese waiting outside impatiently for their exit or to attack without waiting or again, to rob a cemetery at dead of night with a faint light to obtain the larva of a tapeworm? All this many have heard before, but never so fascinatingly described, and, better still, reduced to print for reference so that the gems may be picked out and looked at again and again in the future. The whole is introduced by an excellent reproduction of the oil portrait of Manson by J. Young Hunter. [Might we suggest that more copies of this be produced so that Fellows can procure and frame it without despoiling their copies of the Transactions?]

Sir Philip Manson Bahr's address was followed by others who had known Manson well. Dr Carmichael Low whose association with Manson went back to the last year of the nineteenth century. Dr Hanschell, who was his house-physician in 1910-11 and kept in close touch with him afterwards. Colonel James whose personal contact dated from 1907 but who had corresponded with him from India 8 years before. These all gave their personal reminiscences of Manson a career his personality his foibles. Of his generous help to the earnest student of his benefits to medical education they also spoke, and the last point was stressed by Professor Gordon King who told of Manson's influence on medical education in Hong Kong where his name is perpetuated as the Founder with Sir James Cantlie of the Hong Kong College of Medicine. Truly as the President said at the close of the Session "Manson has left a memory enshrined and enthroned in the hearts of his many pupils for such there is no death."

H. Harold Scott

SCHWERS G. A. Les facteurs de la dénatalité au Congo Belge. [The Causes of Depopulation in the Belgian Congo.] *Résumé des Travaux du Congrès Méd. Congo Belge* 1945 Jan No 3 43-53

In the Belgian Congo anxiety is being felt at the gradual depopulation of certain areas. This depopulation it is considered is due to a lowering of the birth rates and this is evident among some tribes and not among others. One such tribe—the Kunda—which was gradually dying out, was made the object of special study by the author. The results of this study and the theories as to the probable causes of the depopulation are the subject of this article.

Four groups of causes are given. (1) Epidemics, famines wars raids excessive withdrawal of male labour.

(2) Unfavourable biochemical environment "e.g. poor food giving rise to malnutrition.

(3) Chronic infections e.g. venereal diseases

(4) Detribalization and the consequent removal of the control of conduct which tribal rules demanded, and diminishing pride of race.

The author discusses these various causes and, without being didactic, stresses the great importance of the last factor—detribalization.

The idea of the family as a unit has never been recognized by these people. Children belonged to the tribe. The adherence of the individual to the tribal code of behaviour was the guiding rule. When this tribal relationship breaks down, the individual is generally left without any adequate rules of conduct or pride of race. The child, formerly welcomed as a future member of the tribe is now often unwanted and may even be considered an economic handicap to the mother.

The question is however, asked—why do some tribes resist social dissolution better than others? To answer this research not only by medical scientists but also by those interested in other aspects of the problem is required.

Mary G Blacklock

SEVERENS J M & TANNER F W The Inheritance of environmentally induced Characters in Bacteria. *J Bacteriology* 1945 Apr v 49 No 4 383-93 [27 refs] [Summary appears also in *Bulletin of Hygiene*]

Like all populations existing in nature strains of bacteria are of heterogeneous composition in that individuals are not all exactly alike therefore in their investigation of the way in which bacteria become adapted to environmental conditions the authors used single-cell cultures. The bacteria were *Salmonella pullorum* *S schollmüllers* [*Bact paratyphosum* B] and *Eberthella typhosa* [*Bact typhosum*] and the results obtained were similar in all three species.

The cultures were incubated for 7 days at 37°C in broth containing graded concentrations of NaCl, CuSO₄, or HgCl₂ to determine the highest concentration which permitted growth this being judged by the presence of turbidity. After this preliminary determination transplants from single cell cultures were grown in media containing progressively increasing amounts of the respective chemicals in all cases a marked resistance to the chemical was developed—for NaCl 2 to 3 times the highest concentration that allowed growth of the non adapted single cell culture for CuSO₄ it was 4 to 6 times and for HgCl₂ 6 to 12 times. The period of training to maximal adaptation (resistance) varied from 69 to 101 days. A comparison with the non adapted [not exposed to the chemicals] strain was made by plate counts and it was found that growth of the non adapted strains was completely inhibited by concentrations which permitted growth of the resistant strains but the growth of the latter was somewhat retarded by the chemicals. In plain broth the resistant (adapted) and non-resistant (non adapted) strains grew equally well.

The specificity of the resistance was next investigated and it was found that a strain adapted to one chemical was not more resistant to either of the other two chemicals than the non-adapted strain was the resistance therefore was specific in the case of these chemicals but that does not apply of course to other substances such as the sulphonamides which are more closely related to one another.

Single-cell cultures in plain broth were made from the resistant strains and their resistance to the particular chemical was tested from time to time after 18 months propagation involving 55 subcultures and thousands of generations all retained their resistance hence there was no doubt about the inheritance of the resistant characters. The authors point out that the ability of the resistant bacteria to grow as readily as the non resistant ones in plain broth assisted the result since if they had been unable to grow equally well even a low rate of reverse mutation [loss of resistance in relatively few bacteria] would soon have produced a population of non resistant organisms by a process of selection.

The fermentative and morphological characters were unchanged, except that the CuSO₄-adapted cells of *S pullorum* were somewhat elongated.

The mechanism of adaptation—In this experiment it must be assumed that the resistant forms arose either in response to the action of the chemical, or occurred spontaneously and produced a resistant strain by selective action [the non resistant bacteria being unable to compete with them in the environment]. The latter possibility was tested by using agar containing a concentration of the respective chemical which inhibited the growth of the non adapted strain while permitting growth of the adapted strain. This medium was heavily

inoculated with the non-adapted strain and it was found that the strain did contain a few individuals able to grow the results are shown in the table.

Organism	No. of colonies on plain agar	No. of colonies on NaCl agar	No. of colonies on HgCl ₂ agar	No. of colonies on CuSO ₄ agar
<i>S. pallidum</i>	800 000 000	15	21	48
<i>E. typhosa</i>	440 000 000	61	52	30
<i>S. schottmulleri</i>	480 000 000	120	18	29

The colonies on the chemical-containing agar were inoculated into broth containing the highest concentration of the chemicals that had been used and the bacteria grew readily a resistant culture was therefore obtained without a long period of training to become adapted. It is possible that these few cells had a hereditary mechanism which was susceptible to alteration by the chemical and the cells became resistant to it because of this after exposure to the chemical. But whether the cells were resistant before exposure to the chemical or became resistant on exposure to it it is probable that adaptation of bacteria to various environmental conditions consists of selection of such individuals.

The authors conclude that the bacterial variations described in this experiment are best explained by assuming that they are mutations a view supported by the specificity and retention of their chemoresistance.

[The question of variation in bacteria and protozoa is of great medical importance and it appears desirable that more work with single-cell cultures and infections should be done.]

J. F. Corson

HODES P. J. & KEEFER, G. P. Radiology vs. the Monsoon. Effect of Climate upon Equipment. *Radiology* 1945 Mar v 44 No 3 268-72 8 figs

This is a useful article describing in detail the difficulties of diagnostic work in the tropics. The authors appear to have been situated in a valley in India where climatic conditions were exceptionally bad, but their troubles and methods of overcoming them are probably applicable in varying degrees to all tropical areas. They summarize their weather as damp or moist most of the time uncomfortably hot about half the time and very dry about one-quarter of the time.

They found that film which had not been tropically packed showed serious fogging even six to nine months before its expiration date had been reached while film packed in paraffin-soaked cardboard boxes remained in good condition. Their chief film difficulty was mould which developed rapidly after processing and disfigured the film in a few days. This can be avoided by placing the film in 5 per cent. formaldehyde for one minute after processing and then drying it slowly in air.

The developing solutions, freshly and properly prepared were found to be exhausted even before they were used. This was due to organic and inorganic wastes in the water supply and it was not until filtration and settling tanks were added to the water system that this was overcome. Despite these precautions enough silt still remained in the processing tanks to form a scum which had to be carefully removed. Perspiration dripping on screens was also trouble some until the radiographers had been trained to work rapidly and to open the cassettes only a few inches during loading and unloading.

Bulging of bakelite cassettes was overcome by keeping them dry in a well-ventilated, electrically heated, wooden box. Screen blisters were not infrequent

but whether they were due to sweat droplets or humidity alone was never determined. Potter Bucky diaphragms and stationary wafer grids all buckled with the heat even the lead laminations becoming twisted there is apparently no cure for this. Fluoroscopic screens also buckled as the bakelite back warped and allowed moisture in. The authors think but could not prove that the luminescence was affected.

Four of eight shock proof cables broke down always at the cable terminals despite weekly applications of special vaseline at the danger points. This was probably due to moisture and to fluctuations in the primary power supply. Corrosion caused trouble from time to time on all switches meters and connectors and had to be constantly combated by scraping sandpapering and repainting in spite of the fact that thin films of oil were applied frequently to all exposed surfaces. Stainless steel and lead rubber appear to be the only substances unaffected by monsoon conditions. *Peter Kerley*

BULL. AGRIC CONGO BELGE 1941 Dec v 32, No 4 587-639 2 maps (1 folding)
Météorologie du Congo Belge et du Ruanda Urundi. (Meteorology of the
Belgian Congo and Ruanda-Urundi.)

BOOK REVIEW

GUNTHER Carl E. M. [M.D. B.S. D.T.M. (Sydney) etc.] *Practical Malaria Control. A Handbook for Field Workers.* Foreword by Prof. Harvey SUTTON O.B.E. M.D. F.R.A.C.P. B.Sc. D.P.H. F.R.S.I. 81 pp 1944
New York Philosophical Library [15s 6d]

This is not a handbook of malaria control in the ordinary sense in which those words are used. Only thirty of the eighty pages of text are devoted to preventive measures the remainder of the text consisting of accounts of the clinical signs diagnosis and treatment of malaria and its complication blackwater fever. It is written after ten years experience in New Guinea and is intended for those whose work lies in undeveloped districts with widely scattered populations.

The author describes his opinions as radical. On the subject of malaria control they might be better described as conservative. He regards the local elimination of malaria as beyond practical reach except in unusual circumstances and aims rather at the acquisition by Europeans of partial immunity following a reduction in exposure to anophelines by screening and by the siting of dwellings on the lee side of breeding places with an intervening screen of domestic animals and native people and by suppression of attacks with prophylactic quinine. The method of collecting mosquito specimens is described and it is suggested that they should then be sent to some authority for identification and for information on their relation to malaria breeding habits and the best means of combating them as personal enquiry on these points demands more time and knowledge than is possessed by the average medical officer. Some measures of control including the use of fish, the staking of slow rivers the flushing of streams the drainage of swamps and the application of oil and Paris green are described but in no case in sufficient detail to enable the reader to carry out the work without further instruction. An account is given of the screening of houses and the prophylactic use of quinine is described at length. The author

has had such success with quinine that he has not thought it necessary to look further and has therefore little experience of atabrin [mepacrine] and plasmoquine [pamaquin].

In the circumstances of the author a practice there was often little opportunity for the examination of blood films for diagnosis without waste of time which might be dangerous to the patient and he considers that in the field early diagnosis depends on a thorough understanding of the clinical signs rather than on laboratory aids. The clinical forms of malaria are described in detail, and also laboratory methods. Thick films are condemned on account of the necessity to neutralize the water beforehand, but Leishman's stain (with water freshly neutralized with a lithium carbonate solution using brom thymol-blue indicator) is recommended, and the author considers that the ability to perform a reliable leucocyte count is of much more practical value than the more difficult operation of examining a blood film.

The object of treatment is to overcome the immediate attack, and to enable the patient to become "sated" by a subsequent relatively long struggle to maintain control over a chronic infection rather than to eliminate the parasite from the body. Main reliance is placed on quinine, though courses with atabrin alone and with quinine are described. The combination of atabrin and plasmoquine is condemned as intensely poisonous and at least 80 per cent. of patients so treated are said to suffer from cyanosis, severe intractable epigastric pains and extreme mental depression. The section on treatment ends with practical hints on the treatment of malaria in special circumstances, as during pregnancy, lactation and in children. The book ends with a brief account of blackwater fever.

[The author is right to put forward his own views gained by experience. In many ways they do not coincide with those of the reviewer who considers that no handbook for field workers on "Practical Malaria Control" is complete without a working account of at least one method of preventing infection with the disease other than screening and prophylactic quinine.]

G Macdonald

TROPICAL DISEASES BULLETIN

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[No. 11

SUMMARY OF RECENT ABSTRACTS *

IX. LEPROSY

Epidemiology

In reporting two cases of leprosy diagnosed in England HABER (p 1041) makes the point that the disease is not notifiable and that the patients cannot legally be isolated. He thinks that the law should be revised in this respect.

In discussing a case of leprosy in the United States in which diagnosis had been missed for some time, PARK *et al* (p 493) draw attention to the possibility that members of the forces who have served abroad may be infected. The disease should therefore be borne in mind by those called upon to attend returned soldiers.

SOLSONA CONILLERA (p 493) gives an account of leprosy in Spanish Morocco since the first case was found in 1929.

SAUNDERS (p 49) reviews the incidence of leprosy in the Virgin Islands during the last 100 years. There has been a decrease especially since 1900 which is probably due to improvement in social and economic conditions and to isolation of patients which is now fairly complete. In a more detailed study SAUNDERS and GUINTO (p 49) show that incidence in St. Thomas has been very much less than in St. Croix and they attribute this to the higher standard of living in the former. Leprosy is most common in the lower economic groups and house contact is an important factor. SAUNDERS and GIFFEN (p 50) found tuberculoid changes in a high proportion of early neural lesions in the Virgin Islands. They note that spontaneous cure has taken place in several mild neural cases.

In Hyderabad where the purdah system is practised the known incidence of leprosy in males is much higher than in females (RAO p 1041). SANTRA (p 1042) reports a high leprosy rate in Bihar with a fairly even sex distribution but not a high child rate. He (p 1043) has also made leprosy surveys in part of the Bombay Presidency. In this area there is a local custom of isolating leprosy patients in separate rooms of their homes, or outside the villages whatever the type of disease. This custom may facilitate the isolation of all infective persons.

COCHRANE (pp 47-1042) once more points out the great importance of house contact in the spread of leprosy in the part of India investigated 70 per cent.

*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin* 1944 v 41. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

of diseased children were found to have been in contact with infective persons. There is some indication that in villages in which night segregation of infective persons is practised, the incidence of new cases is relatively low. COCHRANE and RAJAGOPALAN (p. 491) have carried out an investigation to determine the relative importance of contact and hereditary susceptibility in leprosy. They found that the incidence of the disease in children living in contact with infective persons not of the same family was quite as high as that in children exposed to infective members of their families and conclude, therefore, that the importance of familial susceptibility is not so great as some authorities suggest. The authors also show that the rate of infection in exposed children is extremely high. In a survey of the work done by the B. E. L. R. A. organization in Madras, AUSTIN (p. 490) makes the point that in one group of child contacts of open cases only 37.3 per cent of the children showed no sign of the disease; some of these may develop lesions later. Voluntary night segregation in the villages is being tried at one rural investigation centre. WALLACE (p. 1044) also stresses the importance of preventing infection in childhood.

DOTLI, *et al.* (p. 48) calculate that the incidence of leprosy in persons living in household contact with infective persons is six times as high as in those not known to have been so exposed; the rate is even higher if the infective person has cutaneous lesions but is lower with neural leprosy. From their work in the Philippines the authors think that males are inherently more prone than females to infection. The commonest age at which leprosy occurs is 10-14 years.

IBARRA PEREZ and GONZALEZ PRIENDES (p. 760) calculate that more than half the leprosy patients in Havana have been infected before the age of 20, mostly in the second decade. Somewhat similar figures are quoted from other parts of the world.

In a lecture on the epidemiology of child leprosy, COCHRANE (p. 579) in addition to the points made above, lays emphasis on the frequency with which early and limited neural lesions in children undergo spontaneous recovery. He also suggests that leprosy bacilli may remain latent for years after gaining access to children, and that active lesions may develop years later when, for some reason, conditions become favourable for multiplication of the organisms.

STEINBERG and MEAGONI (p. 295) have found little evidence of family contact from a study of the case histories of a series of patients, but point out that in one patient who denied any contact a family investigation revealed several cases of demonstrable leprosy. The implication appears to be that families should be closely investigated whatever the statements of patients may be.]

MARIASO (p. 1044) has made a study of marital leprosy at a colony in Brazil.

SAXTRA (p. 1043) investigated two areas in the Central Provinces of India: in one the diet and standards of life are poor, in the other these factors are much better, yet the incidence of leprosy is considerably higher in the latter area. Here the disease is probably increasing, and the proportion of cases in children is higher than in the less affected area. The index of child cases is probably a measure of the tendency towards increase.

Writing of leprosy in West China, CRAWFORD (p. 1041) notes that climatic conditions and diet have little influence on incidence. The disease is largely rural in distribution. DAVEY and ROSS (p. 587) in Nigeria have failed to find that a diet containing large amounts of coco-yam has any effect in predisposing to leprosy. The view that the sapotoxin of this food had that effect was propounded by OBERDÖRFER; it has similarly been disproved for India by LOWE and CHATTERJEE. In an Editorial on diet and susceptibility to leprosy the author (p. 492) sums up the evidence bearing on the subject. This indicates that malnutrition and under-nutrition do predispose to leprosy, but the evidence is not conclusive and further work is needed.

Athology

In a review of attempts to infect hamsters with material from human leprosy lesions BURNET (p 1050) points out that infection is not easy. Such material frequently contains other acid fast bacteria either tubercle bacilli or saprophytic organisms and he states that because these fallacies have not been excluded the experimental production of human leprosy in animals has not yet been proved to have taken place.

LOVING (p 580) has cultivated an acid fast organism from human lepromatous material and from organs of rabbits after implantation of similar material subcutaneously on a culture medium to which thiamin had been added. Details of this medium are given. The organism was apparently identical with the chromogenic acid fast bacillus isolated by Duval.

MOIR (p 582) has investigated the relation between the diffusion factor of Reynals and the bacilli of leprosy. The subject is complicated and the results not consistent but the evidence suggests that *Mycobacterium leprae* has an inhibitory effect upon the diffusion factor. This diffusion (or spreading) factor is present in extracts of animal tissues for instance the skin.

VEGAS and ESPIN (p 581) give details of a method of staining *Mycobacterium leprae* in tissues. This cannot further be abstracted.

Pathology and Clinical Findings

GONZALEZ GUZMAN (p 404) gives the results of a study of the leucocytes in leprosy. There was some tendency towards leucopenia and some deviation of the Arneth Index to the left. DE CAIRES (p 495) has found low haemoglobin levels in leprosy patients in British Guiana, not due to septic complications or to hookworm infestation. He has given iron preparations in addition to the routine hydriocarpus treatment with beneficial results in these cases.

DUBOIS (p 494) records three cases in which lepromatous lesions developed in patients with leprosy of the neural type. This is an unusual course of events.

Bone changes are common in neural leprosy but comparatively rare in lepromatous disease. FAGER and MAYORAL (p 583) think that these changes are not directly due to the leprosy bacillus but are secondary to neurotrophic lesions. There is absorption of bone which generally starts in the distal phalanges and may affect the metacarpals. Trauma is a contributing factor but the main cause is long standing leprous neuritis resulting in disturbance of the nutritional functions of the nerves. There may be leprous endarteritis in advanced cases or in mixed leprosy and in the few bone changes seen in lepromatous cases it is thought that the enlargement of the nutritive canals observed may be the result of this endarteritis. Bone cysts may arise from direct infection of the medullary cavity by *Mycobacterium leprae*. COONEY and CROSBY (p 584) also discuss the question of bone changes and they attribute bone absorption to the combined action of disturbance of circulation anaesthesia and pressure.

GARZON and PITT (p 135) discuss the pathology of caseating abscesses of the nerves in tuberculoid leprosy. These are found in cutaneous branches rather than in main trunks and pathologically the lesions resemble those of tuberculosis. Treatment is surgical.

BOSQ (p 405) reports that he has found leprosy bacilli in macrophages and scales of the superficial layers of the skin. This epidermal elimination evidently needs further study. It appears to be a transient phase in some patients but more permanent in others. DE SOUZA ARAUJO (p 220) describes a method of taking cutaneous lymph for examination in leprosy and refers to the diagnostic and prognostic value of the method.

PARDO-CASTELLO and TIANI (pp. 135-585) have used a modification of the histamine skin test for the diagnosis of leprosy. Intradermally injected histamine fails to provoke erythema in the skin if the sensory fibres of the peripheral nerves which supply the skin are destroyed, but in sensory paralysis due to lesions of the spinal cord, the reaction is normal.

BARROS DE SÁ (p. 403) has found that there is too much variation in the results of the blood sedimentation test, in different patients for it to be useful in diagnosis but he states that a study of the test for each individual patient may have considerable value in enabling an assessment of the progress of the disease to be made.

The question of positive serological reactions for syphilis in the course of leprosy is still a matter of debate. Some authorities consider that a positive test constitutes an indication for antisyphilitic treatment though most agree that positive reactions do occur in leprosy in the absence of syphilitic infection. FAGER and ROSS (p. 1046) have examined 693 patients with the Kolmer or Kahn test or usually both. The proportions positive are much higher in lepromatous and mixed than in tuberculoid and neural cases and observation has shown that the tests tend to become negative as the leprosy progresses towards inactivity or arrest, and *vice versa*. This suggests an antibody in leprosy capable of giving these positive reactions in the absence of syphilis. The authors therefore do not regard positive reactions in leprosy as indication for anti-syphilitic treatment in the absence of symptoms of syphilis. In a small investigation, on the other hand, WENDSOR McLEAN (p. 585) has found no evidence that active leprosy tends to produce a positive reaction to the Kline test.

SOTO (p. 405) discusses the eye complications of leprosy and (p. 406) the methods of treatment that may be used for the different lesions. FRIEL and ZAMBRANO (p. 406) have used thiamin hydrochloride injections in certain eye complications of leprosy—they claim that it has some value.

✓ KEAN and CHILDRESS (p. 60) state that in only 15 of 82 leprosy patients who died could death be attributed primarily to leprosy—tuberculous heart disease, cancer and other conditions were responsible for death in the other cases. MARIANO (p. 221) claims that the notion that cancer is rare in leprosy patients is wrong, and quotes cases in support of his view. [See also KEAN and CHILDRESS above.]

FAGET (p. 296) gives information on the chronicity of leprosy in the patients at Carville, especially in those with the neural type.

GAY PRINCE (p. 586) reports spontaneous cure in a case of leprosy.

Tests.

DHARMENDRA and JAIKARIA (p. 50) have carried out tests with various fractions derived from leprosy bacilli, to find which gives the fewest reactions in non-infected persons. The nucleoprotein extracted by the phosphate-buffer method, in doses up to 0.002 mgm., was the most favourable in this respect, and in that dosage gives positive results in most cases of neural leprosy.

In previous work it has been shown that only the protein fraction of *Mycobacterium leprae* is antigenic in the sense of producing the lepromin reaction. By further work, DHARMENDRA (p. 584) has succeeded in isolating three different proteins, all of which produce reactions (similar to the tuberculin reaction) on intradermal injection in leprosy of the neural type. All, however, give a high proportion of reactions in persons not exposed to leprosy though such non-specific reactions are least with the alcohol-soluble protein. Though a specific test for leprosy infection has not yet been evolved, this result encourages further work. The same author (p. 585) has now prepared a standardized antigen from whole

bacilli derived from leprous nodules. This produces both early and late reactions in neural leprosy and retains most of the advantages of the protein fractions of the bacilli. It does not produce either early or late reactions in lepromatous leprosy. It is more refined than ordinary lepromin and the early reactions are stronger and the late reactions weaker than with lepromin.

DHARMENDRA (p 1050) has been unable to confirm the finding of BERNY and MAUZÉ that an antigen prepared from the urine of bacteriologically positive cases of leprosy is capable of giving positive skin reactions on intradermal injection into persons with leprosy and negative results in persons not infected.

FIELDING and COCHRANE (p 1048) suggest that lepromin should be standardized by counting the leprosy bacilli in the preparations used and make suggestions on suitable techniques.

FIELDING (p 1049) has investigated the action of various lepromins when injected into rats and other animals. The original paper should be consulted for details and for the results of the tests.

In a preliminary report BASOMBRIO *et al* (p 404) produce evidence which indicates that reactions similar to those provoked by injection of whole lepromin can be induced by 2-4 dinitrochlorobenzene. A later report (p 1049) gives details of a considerable number of leprosy patients and contacts tested. In these a very large measure of agreement was found in the reactions to these two totally different substances which brings up the whole subject of the mechanism of the lepromin reaction. BASOMBRIO and MOW (p 1050) record a curious reaction in three stages resulting from the injection of dinitrochlorobenzene in a healthy person.

Treatment

FAGET *et al* (p 494) have published a progress report on the use of Promin in leprosy details of dosage are given. Although as yet no case of leprosy has become arrested the authors show that the drug inhibited the progress of the disease in a fairly high proportion of cases most of the patients showing improvement. Another sulphonamide was also used, but Promin seems to possess to the greatest extent thus far observed some chemotherapeutic properties against leprosy. Anaemia occurs fairly often and may need administration of iron or liver preparations or the administration of Promin may need to be suspended.

BASOMBRIO (p 136) gives to patients in the early lepromatous or tuberculoid stages an intensive treatment comprising large doses of the ethyl esters of chaulmoogra 30 cc. weekly for 7-10 months and shows that good results are obtained in this way.

FIOL and CALCAGNO (p 406) have found some value in a preparation of chaulmoogra and thymol. DHARMENDRA and SANTRA (p 1045) have found that 1 per cent of thymol is effective in place of creosote as an antiseptic in hydnocarpus oil and its esters. The authors give details of the preparation of iodized oil which can be given without trouble by intradermal subcutaneous or intramuscular injection. The iodine appears to have some antiseptic action.

BOSE (p 1046) has used a suspension of bismuth salt in hydnocarpus oil for the treatment of patients with both leprosy and syphilis with some success.

Diphtheria toxoid treatment has been investigated by FAGET and JOHANSEN (p 51) at Carville over a period of a year and with adequate controls. No evidence of benefit was found and the results indicated that lepra reactions and neuritis were increased by the treatment. The authors conclude that this treatment is useless and may be dangerous. SCHUJMAN and MERCAU (p 51) tried diphtheria toxoid in the treatment of 11 cases of leprosy but found no evidence of improvement at any time during the course. IGNACIO CHALA and

LIERAS RESTREPO (p. 587) have added one more to the already long list of trials which have shown that diphtheria toxoid is not useful in the treatment of leprosy. CARPENTER *et al* (p. 52) have failed to find any value in rat leprosy from treatment with diphtheria toxoid. FIOU (p. 407) gives details of the treatment of leprosy carried out at a colony in Argentina. Chaulmoogra preparations are largely used—diphtheria antitoxin has not proved useful.

For the neural symptoms of leprosy ALEXANDER (p. 1048) gives wheat germ flour and ground nuts by mouth daily; injection of magnesium sulphate solution into or around the affected and painful nerves or intravenous sodium bicarbonate solution for neuritis due to the lepra reaction.

MILIK (p. 52) gives details for the treatment of perforating ulcer of the foot—these should be sought in the original.

Control

DAVEY (p. 53) gives an account of the Urukoli Nigerian Leprosy Settlement in which much energetic work is being done. In 1942 there were 44 out-patient clinics round the central colony and 34 model leprosy villages in being or under construction. House-to-house surveys are carried out to detect early cases for treatment which is achieving some success and infective persons are isolated in the villages. MOORE (p. 587) has given an account of two years' work in the Op River leprosy settlement in Nigeria. The object of the settlement is to provide treatment to as many patients as possible, and a large number of clinics have been set up around the headquarter leprosy colony. Records of patients now number over 14,000. In the Settlement most of the patients support themselves and contribute part of their time in unpaid work which greatly reduces the expenses.

Rat Leprosy

BURNET and CARASSO (p. 1051) have studied the effects produced in animals by injections of oil extracts of the bacilli of rat leprosy. Those interested should consult the original abstracts.

DHAKMENDRA and BOSE (p. 538) have shown that sulphapyridine and sulphathiazide have some action in preventing infection when tissues containing rat leprosy bacilli are incubated in dilutions of the drugs at 37°C. and subsequently inoculated into rats.

FRUTKIN (p. 588) has investigated the effect of injections of ascorbic acid on the course of rat leprosy—the results were indefinite. Charles Wilcocks.

MALARIA.

REPT E. A. A Note on *Plasmodium ovale*. *East African Med J* 1945 Mar v 22, No. 3 85-8.

The writer of this note has found that in addition to the three well-known malarial parasites *P. ovale* is quite common at Balovale in the Kaonde Lunda Province of Northern Rhodesia. For the benefit of those who have had little or no experience in the identification of this parasite he has described his method of staining and those features of the parasite which have proved to be of greatest assistance to him. He lays no claim to originality but expresses the hope that his account of the morphology of the parasite may help others to discover it in parts of East Africa in which its presence has not hitherto been suspected. For the identification of the parasite the author finds that thin films stained by

Leishman stain are the best. Thin films stained by Louis Jenner stain and thick films stained by Field's latest double stain have proved disappointing. In thick films it is almost impossible to distinguish the ring stages of *P. ovale* which not infrequently have two chromatin dots from those of *P. falciparum*. [This is quite a useful paper which might well be read by laboratory workers concerned with the identification of malarial parasites.] C M Henyon

SCHÄFFER K. *Plasmodium vivax* und die Feulgensche Nuklealreaktion. [*P. vivax* and the Feulgen Reaction.] *Acta Tropica* Basle 1945, 2 No 1 17-22 3 figs. [10 refs.]

In 1931 PAWAN reported that he had been unable to obtain a positive Feulgen reaction in the chromatin of *Plasmodium vivax* and *P. falciparum*. In the following year BREINDL and JIROVEC reinvestigated *P. falciparum* and found that this parasite gave a positive reaction in the reproducing forms seen in capillaries of the brain. The authors of the present paper have found that the chromatin of the ring forms, schizonts and male gametocytes of *P. vivax* also give a positive Feulgen reaction. It thus appears that the nuclei of malarial parasites are in no way different from other nuclei as the observations of PAWAN had suggested. C M Henyon

COOPER T & WESSELS A L. *Malaria Epidemic Aboard an LST U.S. Nav Med Bull* 1945 July, 45 No 1 54-66 1 fig

During an 8-day period 25 members of a crew of approximately 100 on an amphibious craft fell ill with malaria. Ten days before the first cases occurred the forward sleeping compartments were invaded by a large number of mosquitoes during beaching and unloading operations in an uncontrolled highly malarious area. More than half the men in the first compartments forward were infected. The experience emphasizes the special risks run by landing craft as compared with other naval vessels and the need for good malaria discipline being enforced therein when operating in malarious areas. Protective screening and the regular use of insecticidal sprays are important. Norman White

SHUTE P G. An Investigation into the Number of Sporozoites found in the Salivary Glands of Anopheles Mosquitoes. *Trans Roy Soc Trop Med & Hyg* 1945 July, 38 No 6 493-8.

The investigation described in this paper was undertaken with the object of determining the maximum number of malarial sporozoites in the salivary glands of infected anophelines and the number of blood meals required to deplete the glands of most of the sporozoites. Three experiments were carried out in which the infecting parasite was *P. falciparum* (Rumanian strain) and the mosquito *A. maculipennis* var. *atroparvus*. The day on which sporozoites first appeared in the salivary glands was determined by the dissection of samples from each batch. In one of the experiments this was on the 15th day and in the other two on the 11th day. Following this the batches were allowed to feed on a rabbit every second or third day. In one experiment counts of sporozoites in the salivary glands of 32 mosquitoes dissected on the 4th day after gland infection gave figures varying from 219 450 to 11 450. In another dissections carried out on 11 mosquitoes on the 8th day after gland infection gave figures varying from 209 000 to 950. Dissections carried out later showed that generally up to the 25th day the number of sporozoites per mosquito was fairly well maintained. Following this there was a decline till after about 20 blood feeds most of the sporozoites had been discharged. It seems that there is no uniformity

seconds. Remove the upper urine layer with a pipette and discard. Filter the chloroform layer into a new tube. With a little scoop which holds 0.1 ml. take this volume of silica gel powder and add it to the chloroform extract. Shake for half a minute or until the chloroform is quite colourless, the colour being taken up by the silica. Filter through a fresh paper. Then open the paper allow to dry and match the colour of the silica powder (now pale yellow) against a set of standards prepared by estimating known concentrations of mepacrine. By this technique it is possible to estimate a concentration as low as 0.1 mgm. per litre. To measure lower concentrations repeated 5 ml. samples of urine are extracted by the same sample of chloroform until a measurable colour is obtained.

Method II.—Into a test tube, marked at 10 ml. pour urine up to this mark. With a scoop which delivers the appropriate amount add 0.25 ml. of silica gel. Shake frequently for 8 minutes and then stand for two minutes. Pour off all the urine and add 5 ml. of water. Shake and stand for 1-2 minutes. Add 1-2 ml. of water and with it wash the silica gel into a folded filter paper. When the water has drained away place the filter paper on a fresh piece of paper and open it. With a knife scrape the silica gel off on to a third piece of paper and allow it to dry. Then scrape it into a small heap and compare the pale yellow colour of the silica gel with standard cards prepared to match the different concentrations of mepacrine. This method will measure concentrations as low as 0.5 mgm. per litre. Silica gel is not suitable for urines which contain bile pigments.

Method III.—Use is made of paper containing 20-40 per cent silica gel. Samples of this were prepared by Messrs Cross & Bevan. Pour 5-10 ml. of urine into a test tube. Put in a strip of the paper and allow to stand for two hours shaking every 15 minutes. Remove the paper and dry it by pressing between two filter papers. Then compare it with standards. This method is less sensitive than the others. It is effective in the range 1 to 10 mgm. per litre.

The silica gel powder is the kind supplied in granules for dehydration purposes. A sample with very white granules should be used. The granules should pass a 60 mesh but not a 120 mesh. Suitable powder can be obtained from Messrs Silica Gel Ltd. Aldwych House London, W.C.2. The scoops are made by drilling a hole into a small piece of hard wood. Coloured standards can be prepared by carrying out estimations on known concentrations of mepacrine. Standard cards may also be obtained from the Editor of the *Journal of Tropical Medicine and Hygiene* F. Hawking

WAR DEPARTMENT TECHNICAL BULLETIN. Wash., D.C. 1945 July 23 pp. 4 figs.
Data on Malaria Control. [TB Med 182. Restricted.]

BROOKE M. M. Effect of Dietary Changes upon Avian Malaria. *Amer J Hyg* 1945 Jan. v. 41 No. 1 81-108 6 figs. [20 refs.]

With the object of discovering if the course of a malarial infection is influenced by deficiencies in diet experiments were carried out on canaries, pigeons and ducks suffering from *P. relictum*, *P. cathemerium* or *P. lophurae*. After being fed for some time on a stock diet which was shown to be adequate for the maintenance of health certain birds in each batch were either deprived of part of their daily allowance of stock diet so that they were undernourished or they were given one of several experimental diets in place of the stock diet. One of the experimental diets was deficient in vitamin B₁ while the others were rich in carbohydrates and low in practically all other nutritional values as compared with the control diet. It was supposed that these deficient diets were to some extent comparable with the diet of many people in malarious regions of the southern United States and other countries. As the change over from the stock

diet to an experimental one adversely affected the appetite of the birds it appeared evident that they suffered from undernutrition as well as from malnutrition. The birds were inoculated with large doses of malarial parasites and the effect of the resulting infection was gauged by the severity of the symptoms and the intensity of the parasitaemia determined by daily counts of the parasites the number of days during which parasites remained in the blood and the course of the infection as revealed by graphs of the daily counts. The effect of the experimental diets on latent infections was measured by the reappearance or not of malarial parasites in the blood and the intensity of infection resulting from a reinoculation of malarial parasites.

In general the effect of the experimental diets was to cause the birds to suffer from more severe primary attacks to reveal a greater tendency to relapse and a reduced resistance to superinfection. There were more fatal infections among the birds on the poor diet and the symptoms of the malarial attacks were more severe. As regards birds with latent infections parasites reappeared in the blood only in the case of those placed on experimental diets. A group of pigeons with latent infections did not show any sign of relapse or lowered resistance to superinfection when placed on a diet deficient only in vitamin B₁. Immunity to superinfection was greatly reduced or entirely lost by over one third of the birds with latent infection when given the experimental diets. One of the birds on the stock diet was successfully superinfected but it showed a greater resistance to this infection than did superinfected birds on experimental diets. [Compare the findings of PASSMORE & SOMMERVILLE in monkeys maintained on deficient diets the results did not indicate any difference from the normal in reaction to malaria infection see this *Bulletin* 1941 v 38 646] C M Wenyon

HAAS V H FELDMAN H. A. & EWING Frances M. Serial Passage of *Plasmodium gallinaceum* in Chick Embryos. *Pub Health Rep Wash* 1945 May 25 v 60 No 21 577-82 1 pl

Fertile eggs are incubated for 11-12 days. 0.1 cc. of blood containing *P. gallinaceum* obtained from an infected chick or embryo is injected intravenously by the technique of EICHORN (*Science* 1940 Sept 13 245). After 5-6 days blood from the embryos is examined. Suitably infected embryos are selected and their blood is collected with an anticoagulant for infection of more embryos. The strain has now been maintained for 14 passages. During the first 12 passages 751 embryos were inoculated. 41 were sacrificed for examination. 281 (39 per cent) died in the first 48 hours presumably from the trauma of inoculation. 145 died at the ninth day only 19 survived to hatch out and the remainder died at intermediate times. By the eighth day 80-90 per cent of the erythrocytes contain parasites. Infected embryos develop a green discoloration of the membranes amniotic fluid, yolk, liver and spleen. It begins about the 4th day and becomes heavy after the 6th day. This green discoloration is diagnostic of malarial infection. F Hawking

- i. COATNEY G. R. COOPER W. C. & MILES V. I. Studies on *Plasmodium gallinaceum* Brumpt. I. The Incidence and Course of the Infection in Young Chicks Resulting from Single Mosquito Bites. *Amer J Hyg* 1945 Jan. v 41 No. 1 109-18. [16 refs.]
- ii. ——— & TREMBLEY Helen L. Studies on *Plasmodium gallinaceum* Brumpt. II. The Incidence and Course of the Infection in Young Chicks following the Inoculation of Infected Salivary Glands. *Ibid* 119-22.

(i) During the course of experimental work with *P. gallinaceum* the authors had occasion to attempt infection of over 300 chicks under two weeks of age

by the bites of single infected *Aedes aegypti*. Of these chicks 290 survived long enough to be considered from the malarial point of view and 248 (85.5 per cent.) became infected. The mean of the prepatent period between the mosquito bite and the appearance of parasites in the blood was 8.63 ± 0.162 days. Of the 248 infected chicks, 84.3 per cent. died and all but one of these showed exoerythrocytic schizonts in the brain. The peak of the infection was reached within the first seven days after the first appearance of parasites in the blood. The mean of the peak parasite counts was 4120 ± 214 parasitized cells per 10,000 red blood corpuscles. The mean survival time of the birds that died was 13.36 ± 0.208 days from the time of the mosquito bite. The younger the chicks the shorter was the course of the infection and the higher was the mortality rate. The authors conclude that this infection in young chicks is very suitable for chemotherapeutic studies. On the other hand they think that for inducing the infections mechanical injection of sporozoites may be more satisfactory than the feeding of infected mosquitoes.

ii. In the second paper the authors review the results they have obtained in the inoculation of 200 chicks under a week old with the isolated salivary glands of *Aedes aegypti* infected with *P. gallinaceum*. The infection rate of 97.5 per cent. is considerably higher than in the previous series in which chicks were exposed to the bites of single infected mosquitoes. Of the chicks that became infected 191 (97.9 per cent.) died and of 182 examined all showed exoerythrocytic forms in the brain. The mean duration of survival of those that died was 12.05 ± 0.163 days from the time of inoculation. The mean prepatent period was 8.523 ± 0.108 days. The peak parasites averaged 3,776 per 10,000 red blood corpuscles. It was found that the mechanical introduction of infected salivary glands was tedious and time-consuming though highly effective. To simplify matters injection of comminuted whole mosquitoes was tried. This was found to be so satisfactory that the procedure has been adopted as the routine method of producing infections. C. M. Wenyon

GUTIERA, F. BELTRÁN E. DE LA GARCIA, F. & LARRENA, M. R. La acción del yodobismuto de sodio sobre el paludismo aviario. (*Plasmodium gallinaceum* Brumpt, 1935) [Action of Sodium Iodobismuthate on Bird Malaria.] *Rev. Ind. Salubridad y Enfermedades Trop. Mexico*, 1944 Mar. v 5 No 1 59-68. [14 refs.]

The authors have tested the action of sodium iodobismuthate on *Plasmodium gallinaceum* infection in young chickens. In one series of ten chickens the daily injections commenced on the day parasites were inoculated (protective treatment) while in another series they were commenced on the sixth day after inoculation (curative treatment). The mortality rate in untreated infected birds was 100 per cent. the average duration of life being 19.1 days. In uninfected birds the administration of 0.03 cc. of the solution of the drug (representing 0.0022 gram) daily for six days apart from the local irritation gave rise to generalized toxemia, which brought about a mortality rate of 20 per cent. during the prescribed observation period of 60 days. When 0.5 cc. of a 1 per cent. solution of quinine hydrochloride (50 mgm. per kilo. of body weight) was injected daily for the six days following inoculation, the infection was retarded while the drug was given but it developed rapidly after this giving a mortality rate of 90 per cent. and an average life of 27.2 days. When 0.02 cc. of the solution of sodium iodobismuthate was given similarly there was a longer delay in the infection and a reduced mortality rate of 70 per cent. with an average life of 32.3 days. In the series in which treatment with sodium iodobismuthate was not commenced till the sixth day after inoculation (in this case 0.03 cc. daily for six days) though the infection was less intense than in controls which received no treatment, there was a mortality rate of 100 per

cent. with an average life of only 15.7 days which is considerably less than in the untreated controls. It seems clear that when treatment is commenced at the time of inoculation the drug has a definite action in reducing the infection and prolonging life.

C. M. Wenyon

WOLFSON Fruma. An Experimental Study of Mixed Infections with *Plasmodium cathemerium* and *Plasmodium lophurae* in Ducks. *Amer J Hyg* 1945 Jan. v 41 No. 1 123-35 4 figs [13 refs.]

Observations on human malaria have generally shown that in cases of mixed infections there is some degree of antagonism between the species of parasite present. Very little being known of the behaviour of avian malarial parasites in mixed infections the author decided to investigate in ducks mixed infections of *P. cathemerium* and *P. lophurae*. These were produced by the intravenous inoculation of a mixture of two infected bloods in such proportion that each duck received three billion parasites of each species per kilogram of its body weight [In American measurement one billion is 1 000 millions. At the same time control birds were inoculated with each species separately. A comparison of the course of the infections in the control birds with that of the mixed infections showed that in the mixed infections each parasite developed independently of the other and that the number of parasites present at any time agreed fairly well with the sum of the numbers of parasites present in controls. Furthermore the degree of preference of *P. cathemerium* for reticulocytes which is a striking feature of this parasite was the same in the birds with mixed infections as in the control birds just as in the mixed infections the proportion of mature erythrocytes infected with *P. lophurae* which this parasite prefers was the same as in the controls.]

Having produced the mixed infections the author attempted to separate the parasites. It was observed that in the control birds the peak of *P. cathemerium* infection was reached on the third day while that of *P. lophurae* infection was on the fifth day. Accordingly subinoculations of 3 billion parasites per kilogram of body weight were made from cases of mixed infections on the third and fifth days. As was anticipated, one infection was predominantly *P. cathemerium* while the other was predominantly *P. lophurae*. The purity of these infections was then tested by inoculation into birds with latent infections of one or other of the parasites. The inoculation of the predominantly *P. cathemerium* infection into birds with a latent infection of the same species resulted in the development of a mild *P. lophurae* infection only the birds showing a high degree of resistance to *P. cathemerium*. Similarly ducks having a latent infection of *P. lophurae* were inoculated with the predominantly *P. lophurae* infection. This resulted in what seemed to be a mild *P. cathemerium* infection. The supernatant experiments tended to indicate that the attempts to isolate pure infections from the mixed infections had to a large extent been successful. An outcome of these subinoculation experiments is that if subinoculations of a mixed infection of the two species is made every three days or twice weekly pure infections of *P. cathemerium* will ultimately be realized. It is suggested that by regulating the dose of each species inoculated it might be possible to arrange that equal numbers of each species would be present in the blood on a certain day. Such a mixed infection might be employed for testing the effect of drugs on both species in one host.

C. M. Wenyon

BALL E. G. ANFINSEN C. B. GRISMAN Q. M. NICHIE R. W. & ORMSBEE R. A. In Vitro Growth and Multiplication of the Malaria Parasite, *Plasmodium knowlesi*. *Science* 1945 May 25 542-4

Two techniques are described. In one a small volume of lightly infected blood is diluted with three volumes of a very complex nutrient medium

the container is gently rocked and a slow stream of air with 5 per cent. carbon dioxide is passed through it. In the second technique the infected blood is separated from a slow stream of nutrient medium by a cellophane membrane. In both cases the temperature is 38.5°C. Cultivation is carried out for periods of 24 hours if longer periods are required, subcultures are made into fresh uninfected blood and fresh medium. In 89 experiments the average multiplication of parasites during 24 hours has been three- to four fold, which is approximately the same increase as that which occurs in the blood of monkeys. During the 24 hours, the usual periodic change in the percentages of the different stages of the parasites can be seen. Parasites have been successfully cultivated for six days, after which they were still able to infect a monkey. Various biochemical studies have been made on the metabolism of the plasmodia. One of the essential constituents of the nutrient medium is proteose-peptone possibly it acts by supplying *p*-amino benzoic acid.

[Only a brief abstract of the provisional report of this important work has been given here since it is hoped that a full account will soon be published.]

F. Hawking

VENEZUELA. MINISTERIO DE SALUD Y ASISTENCIA SOCIAL. DIRECCIÓN DE SALUBRIDAD PÚBLICA. División de Malaria. Curso de Malaria. [Course in Malaria. I & II. Cyclostyled 1944 Maracay, Aragua, Venezuela.]

In two bound volumes the Division of Malaria of the Public Health Department of Venezuela has published the instruction papers issued to students who attended the course on malaria held at Maracay from 2nd October to 1st December 1944. The general direction of the course was entrusted to Professor Arnaldo GABALDON and he was assisted by a large staff of medical men and engineers.

The papers included in these volumes are cyclostyled copies of typescript, reproduced on one side of the paper only. They form a very complete survey of the whole subject. The student who masters all this information will certainly be well able to undertake any kind of work which relates to malaria. The volumes are divided into the usual sections—protozoology, entomology, clinical matters, epidemiology, control, etc. notable features are the instruction given in haematology, statistical methods and engineering. The whole work is, of course written in Spanish. It provides an interesting prospectus of the instruction given and could with advantage be consulted by those in charge of similar courses elsewhere.

Charles Wilcocks.

TRYPANOSOMIASIS

BURT E. Hypertrophied Salivary Glands in *Glossina*. Evidence that *G. pallidipes* with this Abnormality is peculiarly suited to Trypanosome Infection. *Ann Trop Med. & Parasit.* 1945 May 31 v 39 No 1 11-13.

Hypertrophied salivary glands, brown, sack-like and coarse in texture as viewed with the low power of the microscope and some four times the normal width have been found in *Glossina pallidipes* and *G. morsitans*. In the former these were found in 2-3 per cent of flies but in the latter fewer than one per thousand. Among 1129 *G. pallidipes* dissected, 32 had hypertrophied salivary glands seven had trypanosome infections, three of these being in the group with enlarged glands. The *G. pallidipes* with hypertrophied glands thus appear particularly suited for the development of trypanosomes, notably for *T. brucei*. No evidence for this was obtained with *G. morsitans*. I. B. Wigglesworth.

POTTS W H & VANDERPLANK F L. Mode of Entry of Contact Insecticides [Correspondence.] *Nature* 1945 July 28 112

Tsetse (*Glossina* spp) were allowed to settle on the dry haired surface of pieces of cattle hide which had been treated with various strengths of DDT (or pyrethrum) or the flies were held over the surface so that only their feet touched it. The drugs were applied in various adhesive solutions—gum serum wax resin &c—and the skin dried afterwards. The flies were killed—in a few seconds by pyrethrum and in about half an hour or more by DDT—the latter caused convulsive movements of the legs so mechanical conveyance to the spiracles could not be excluded but the action of pyrethrum was too rapid for this to occur. It is unlikely that any emanation could have entered the spiracles and the results suggest that the insecticides were absorbed through the cuticle of the pulvilli in the case of DDT this would probably have great practical importance. J F Corson

RODHAIN J & VAN GOIDSENHOVEN C. Persistance prolongée de sensibilisatrice fixant l'alexine après guérison de la trypanosomiasis [Persistence of Complement-fixing Antibodies after Cure of Trypanosomiasis.] *Ann Soc Belge de Méd Trop* 1944 Dec 31 v 24 No 4 235-46

The authors have previously recorded the presence of complement fixing antibodies in the blood and cerebrospinal fluid of patients in the advanced stage of trypanosomiasis [this *Bulletin* 1943 v 40 120] they now present observations made on one of those patients during four years and also some experiments on a goat and a ram both infected with *Trypanosoma rhodesiense*. The antigen used was made from *T. equiperdum* (occasionally one from *T. rhodesiense* was used for comparison) a positive serum of a rabbit infected with *T. equiperdum* was used as a control in the tests.

In March 1941 the patient was clinically cured and his cerebrospinal fluid had become normal both serum and cerebrospinal fluid however gave a positive complement fixation reaction. The serum was also positive in three later tests—on 21 7 41 10 3 42 and 1 3 43—while the cerebrospinal fluid gave a negative reaction on the two former dates and a positive one on the last remaining normal otherwise. In May 1945 the patient was in excellent health.

The tests made on the goat and ram showed that the serum gave a positive reaction over one year after treatment in the goat was at first positive with germanin. The cerebrospinal fluid of the goat was not tested. These results differ from those of VAN DEN BRANDEN [this *Bulletin* 1942 v 39 237] who found that the serum in rabbits infected with *T. brucei* gave a negative reaction within three weeks after treatment with moranvil [Germanin].

The complement fixation reaction was apparently not affected by the presence of germanin in the blood. These observations show that the persistence of the reaction after appearance is not an indication for the continuation of treatment J F Corson

CHEE G GELLING E M. K. & MACHATTON R M. Trypanocidal Activity and Toxicity of Antimonials. *J Infect Dis* 1945 Mar-Apr v 78 No 2, 144-51 3 figs. [15 refs.]

— & —. The Effect of Cysteine on the Trypanocidal Activity and Toxicity of Antimonials. *Ibid* 152-4

The aim of this investigation was to find a simple quantitative method for assay of trypanocidal activity of antimonials and to compare this property.

as well as toxicity in the case of certain established preparations of antimony. The pentavalent compounds used were stibamine, stibemyl, neostibosan and neostam as well as the trivalent types tartar emetic, antimony sodium thioglycollate, antimonythiomalate and fousadm. Mice were injected with 500 000 trypanosomes (*T. equiperdum*) intraperitoneally whereby a moderate blood infection was produced 24 hours later. The aqueous solution of the drug was then injected intramuscularly to batches of ten or more mice in a single dose if tolerated, or in three divided doses on successive days if the single large dose proved too toxic. In the first method of assay that of suppressive therapy the trypanocidal activities of the antimonials were compared by the amount of each drug which gave rise to an increase in the survival time of treated mice equal to that of the life-span of untreated controls (generally two days). This quantity of drug was regarded as having 100 per cent suppressive effect and was termed the standard suppressive dose. It was found that the suppressive effect of three of the trivalent compounds was the same while the fourth, fousadm was somewhat less active. The four pentavalent compounds showed equal activity which was about 1/10 that of tartar emetic. In the second method of assay in which curative therapy was employed, results were similar to those obtained by the first method. Determination of the value of the therapeutic index for each antimonial, based on the ratio of median lethal dose to median curative dose shows that it is generally higher for the pentavalent compounds, while that for tartar emetic was lowest of all.

II. VORGILO and co-workers (this Bulletin 1924 v 21 414) found that certain substances containing the SH group were able to counteract the toxic effect produced by arsenoxide on trypanosomes and a representative mammal. LATYON (C. R. Acad. Sci. 1834 v 189 646) showed that cysteine also reduced the toxicity of antimony thiomalate for mice. In view of these findings the present authors have sought information on the mechanism of action of antimonials on protozoa, along similar lines. They investigated the effect of cysteine on the trypanocidal activity and toxicity of tri- and pentavalent antimonials. These substances for which the median lethal dose, standard suppressive dose and median curative dose had been determined in mice infected with *T. equiperdum* (see preceding abstract) were injected intramuscularly. A solution of cysteine hydrochloride previously neutralized with tri-sodium phosphate was injected into a different muscle. It was found that the toxicity of the four trivalent antimonials used above was reduced to a marked degree while that of stibemyl, stibamine and neostibosan was unaffected. Analogous experiment showed that the trypanocidal power of the trivalent compounds, but not that of pentavalent derivatives was also reduced by cysteine. The authors believe as previously suggested for trivalent arsenicals that combination of the drug with sulphhydryl groups may take place. Cysteine was also found to antagonize the inhibition of glucose breakdown by trypanosomes *in vitro*.

J. D. FALLON

BESSEMAN, A. & DEROM, R., with the assistance of P. DOUSSY, Mlle. H. BARR & J. STETAKY. Trypanosomes et pénicilline. [Trypanosomes and Penicillin.] Ann. Soc. Etude de Med. Trop. 1944 Dec. 31 v 24 No 4 181-4 [10 refs.]

The authors tested the action of sodium penicillin on *Trypanosoma congolense* *in vitro* and *in vivo*. They incubated mixtures of equal parts of heavily infected defibrinated guinea-pig blood and various concentrations (0.1, 1, 10, 100 and 1 000 Oxford units per cc. in normal saline) of sodium penicillin at 37°C. During the first hour the 1 000-unit mixture alone showed more immobilization and

lysis of trypanosomes than the control but after one hour both the test and the control tubes showed equal numbers of living trypanosomes.

The mixtures of blood and penicillin were injected subcutaneously into guinea pigs all died of trypanosomiasis except those which received the 1 000-unit mixtures after three hours incubation these were not infected.

Infected mice and guinea pigs were injected intramuscularly every three hours with sodium penicillin (200 and 1 000 units) the mice were given these injections for 11½ days and showed no ill effects but the guinea pigs all died between the 3rd and 6th days while control infected guinea pigs only died of their trypanosomal infection. Two uninfected guinea pigs also died on the 4th day of the same course of penicillin injections. No effect of penicillin on the numbers of trypanosomes in the peripheral blood was observed either in mice or guinea pigs.

The authors observe that while rabbits tolerate intramuscular injections of 5 000 units of sodium penicillin given 3-hourly for 8 and 19 days and mice tolerate 200 units 3-hourly for 8 and 11½ days guinea pigs cannot tolerate a corresponding dosage.

J F Corson

VAN DEN BERGHE L. La trypanosomose de poussins éclos après inoculation chorio-allantoïdienne. [Trypanosomiasis in Chicks hatched after Inoculation into the Chorio-Allantoic Membrane.] *Ann Soc Belge de Méd Trop* 1943 June 30 v 23 No. 2, 113-39 1 graph & 2 figs on 1 pl.

It is known that while adult fowls are highly resistant to infection with pathogenic mammalian trypanosomes it is comparatively easy to infect chick embryos which rapidly succumb to the infection.

In the present paper the author records experiments which throw light on the mechanism determining the susceptibility of the fowl at different stages of its development. In the course of this investigation about 200 chick embryos were inoculated in the chorio-allantoic membrane with *Trypanosoma evansi*. It was demonstrated that the chick embryo is highly susceptible to infection between the 8th and 14th days of incubation whereas inoculations made between the 15th and 17th days fail to produce an infection. In positive cases the trypanosomes make their appearance in the blood of the embryo on the 4th day after inoculation after which they increase in numbers up to the 7th day eventually killing the embryo by the 8th or 9th day. Thus as a rule infected embryos perish before they can hatch. The author attempted to retard the course of infection in the embryo with a view to bringing about the hatching of infected chicks. He succeeded in three cases in all of which the embryos had been inoculated on the 10th day of incubation while the appearance of trypanosomes was deferred to the 7th or 8th day after inoculation. In the chicks the trypanosomes persisted for a short time only gradually decreasing in numbers and disappearing entirely six to nine days after hatching. The chick thus rapidly becomes resistant to trypanosome infection.

In vitro tests showed that the serum of normal fowls and of fowls reared from infected chicks was markedly trypanocidal whereas the effect upon trypanosomes of serum taken from chick embryos was only slight or was absent altogether. The age-difference in the resistance to trypanosome infection manifested by chicks appears to be similar to that observed in rats infected with *T. lewisi*; while young rats rapidly succumb to the infection, in adult rats the trypanosomes are gradually eliminated, owing to the development of specific ablastic and trypanolytic antibodies, the former inhibiting reproduction of the parasites the latter subsequently destroying them.

C A Hoare

RODHAIN J & VAN DEX BERGHE L. Inoculations de spirochètes et de protozoaires sur membrane chorio-allantoïdienne de poulet. [Inoculation of Spirochaetes and Protozoa into the Chorio-Allantoic Membrane of the Chick Embryo] *Ann. Soc. Belge de Méd. Trop.* 1943 June 30 v. 23 No. 2, 141-56. [19 refs.]

Before proceeding to tell of their own experiments the authors review the results obtained by other workers in the cultivation of spirochaetes and protozoa in the chorio-allantoic membrane of the chick embryo. A list of organisms used and the results obtained up to date by various observers is adduced.

The present authors have succeeded in infecting chick-embryos with the following organisms: *Borrelia* (= *Spirochaeta*) *duttoni*, *Trichomonas foetus*, *Leishmania infantum*, *Trypanosoma cruzi*, *T. brucei*, *T. gambiense*, *T. evansi*. However they failed to produce infections with the following: *Treponema reutiliae*, *Plasmodium gallinaceum*, *Trypanosoma respirationis*, *T. pipistrelli*, *T. seimuri*, *T. rotatorium*, *T. fringillae*, *T. congolense*. As a rule the eggs were inoculated on the 10th day of incubation.

It is noted that all the pathogenic forms—with the exception of *Plasmodium gallinaceum* and *Trypanosoma congolense*—were able to grow in the chick embryo whereas all the non-pathogenic forms, without exception failed to produce an infection. It is noteworthy that none of the organisms capable of developing in the embryo is infective to the adult fowl. The reverse is true for *Plasmodium gallinaceum* to which the chick is highly susceptible while the embryo is refractory. The resistance of the adult fowl to infection with certain micro-organisms is attributed to immunity which is apparently absent from the embryo but develops in the young chick after hatching. C. A. Hoare

CHEN G. GEILING E. M. E. & MACHATTOA R. M. Parasitaemia and Length of Survival of Mice Infected with *Trypanosoma equiperdum*. *Amer. J. Hyg.* 1945 Mar., v. 41 No. 2, 221-7. 3 figs.

The investigation forming the subject of this paper was carried out to determine the relationship between parasitaemia, survival time and the inoculating dose of *Trypanosoma equiperdum* in mice. Each experimental mouse was inoculated with 0.5 cc. of saline-glucose suspension containing a measured number of trypanosomes counted in a haemocytometer. This is a highly technical statistical study which should be consulted in the original. The results are summarized as follows:—

The individual variation in the survival time of mice infected with *Trypanosoma equiperdum* was found to be independent of the inoculating dose of trypanosomes. The length of survival and the logarithm of inoculating dose as well as the logarithm of parasitaemia and the duration of infection are linearly related. Empirical formulae were derived from which the survival time or degree of parasitaemia may be calculated from the inoculating dose of trypanosomes.

C. A. Hoare

ELKES G. Experimental Studies and Critical Considerations regarding the Life Cycle of *Trypanosoma cruzi*. *Amer. J. Trop. Med.* 1945 Mar. v. 25, No. 2, 141-3. [10 refs.]

This is a critical consideration of the life-cycle of *Trypanosoma cruzi* in which the author finds himself at variance with some of the generally accepted views, according to which the development of *T. cruzi* proceeds as follows. In the vertebrate host the blood-form is represented by the characteristic trypanosome stage which does not multiply in the blood but from time to time the trypanosomes penetrate into various tissues (especially muscle fibres) where they

become rounded into leishmanial forms. These reproduce by repeated binary fission finally giving rise to flagellated forms of the crithidial type which are transformed into trypanosomes again. These flagellates reappear in the blood stream as slender trypanosomes which gradually become broader assuming the typical structure of the adult blood form. When taken up by the invertebrate host the blood trypanosomes are transformed into crithidia which multiply in the gut and finally give rise to metacyclic trypanosomes. These constitute the infective stage and are voided with the faeces of the bug. When inoculated into the vertebrate host the metacyclic trypanosomes do not directly invade the blood but first multiply in cells of the reticulo-endothelial system as leishmanial forms and later develop into the slender trypanosomes which find their way into the blood.

The author doubts whether the slender trypanosomes (which he erroneously calls metacyclic) are transformed into the adult blood trypanosomes. From a study of artificial cultures he believes that the trypanosome form originates from a direct unrolling from the round [leishmanial] form without other intermediate flagellate pre stages. He even denies the existence of a crithidial stage in the development of *T. cruzi* in the vertebrate host though admitting that the trypanosomes may sometimes originate from crithidia if the latter has previously undergone a ripening process generally combined with a multiple segmentation of the nuclei. However this is by no means the only or most frequent mechanism in the evolution of the trypanosome form. Processes as yet not fully explained, lead to the formation of micro-leishmania and elementary nuclei pairs which in turn develop directly into the trypanosome. As to the transformation of the trypanosome stage to the leishmanial stage this is termed retrogression and is said to lead to the minute round form which possibly represents a resting stage. The author also believes in the existence of sexual processes in *T. cruzi*.

[From the quotations given above it is evident that the opinions expressed in this paper are very unorthodox and conflict with the views held by most competent students of *T. cruzi*. They are moreover highly speculative while the arguments adduced in their support are unconvincing and sometimes even incomprehensible. Furthermore the author's methods of observation are also open to criticism. Thus his views regarding the developmental stages of *T. cruzi* in the vertebrate host are based on a study of artificial cultures. In these as is known the development of trypanosomes is similar to that in the vector and is therefore not comparable to the stages observed in the vertebrate host.]

C. A. Hoare

ROMANA C. Infección por *Schizotrypanum de murciélagos argentinos* [Infection of Argentine Bats with *Schizotrypanum*.] *An. Inst. Med. Regional Tucumán*. 1944 Sept. v. 1 No 1 93-104 4 figs

Trypanosomes infecting Chiroptera are of particular interest because of their strong morphological resemblance to the *T. cruzi* of man. The author has examined 331 specimens of bat belonging to 12 species [but in four species only were more than ten examined] and his findings were as follows. Of 186 *Tadarida brasiliensis* four were found infected all in the same dwelling but caught at different times of 44 *Desmodus rotundus rotundus* none of 47 *Myotis nigricans* none of 15 *Histiotus laephotis* two of 5 *Eptesicus fuscus* three. None of the other seven species. *Enemops perotis*, *Promops ancilla*, *Cynomops cerastes*, *Molossops temminckii*, *Molossus rufus*, *Dasypterus ega argentinus* and *Lasiurus borealis varius* was found positive. *Histiotus laephotis* has previously been found infected by MAZZA in 1940 [this Bulletin 1941 v. 38 315] but the other two have not. Xenodiagnostic and

inoculation tests were tried but with uniformly negative results. From a study of the measurements and morphological characters of the trypanosomes seen they belong to the type *resperiliosis*. [This is one of the four types into which E. DIAS has divided the group *Schizotrypanum* the others being *S. phyllostome*, *S. lastatus* and *S. cruzi* (see TORANZOS L. B. below). Further study is needed to determine whether or not they are the same as *T. cruzi*.]

H. Harold Scott

TORANZOS L. B. La infestación del *Triatoma* (*Edriatoma*) *rubrovaria* por el *Schizotrypanum cruzi*—su comprobación en la República Argentina. Infection of *Triatoma rubrovaria* by *T. cruzi*. *An. Inst. Med. Regional Tucumán*, 1944 Sept. \ 1 No 1 105-16 4 figs.

Finding *Triatomidae* infected with *T. cruzi* is always a pointer to the probability of Chagas' disease in man in the district. In Mercedes a department of the province of Corrientes specimens of *T. rubrovaria* have been captured harbouring a trypanosome. For relegating these to a group DIAS has made measurements and decided that the ratio of the distance between the middle of the nucleus and the posterior extremity to that between the same spot and the anterior extremity is of great value. This ratio he calls the Dias-Freitas Index and by its means he has named four types of *Schizotrypanum* namely *S. resperiliosis* with index 2.6 μ , *S. cruzi* 1.6 μ , *S. phyllostome* 1.4 μ and *S. lastatus* 1.0 μ . That found in *Triatoma rubrovaria* has an index 1.8 μ approximating that is to *T. cruzi*. It is easily cultivable on N \ \ medium is virulent for the white mouse, the guinea pig, the dog and *Ctenomys tucumani* a rodent of the cane-fields and numerous in parts of the Argentine.

Of 202 specimens of *T. rubrovaria* ten (4.9 per cent.) were positive. It lives in quarries and, according to the quarrymen it is very voracious biting day and night especially in summer. Female *Triatoma* are more often infected than are males. Of 33 females examined three were positive. Of 75 males none but of 30 in the nymph stage ten were positive.

H. Harold Scott

ROMAÑA, C. & COSSIO, F. Formas crónicas cardíacas de la enfermedad de Chagaa. [Chronic Cardiac Conditions in Chagas's Disease.] *An. Inst. Med. Regional Tucumán*, 1944 Sept. \ 1 No 1 9-31 50 figs. [28 refs.]

This is the first issue of a new publication from the University of Tucumán the aim of which is to report the results of investigations into the "regional pathology and experimental medicine connected therewith and social hygiene."

The opening paper is a dissertation on cardiac conditions in Chagas's disease based on 35 detailed cases selected from 100 under the authors' observation. They have met with a surprisingly large number of cases of heart lesions associated with *T. cruzi* in Brazil and the Argentine—patients with subjective symptoms palpitation, fatigue precordial pain and distress even actual angina pectoris, vertigo and syncopal attacks and objectively affections of conductivity excitable action, extrasystoles tachycardia, fibrillation, etc. Laboratory diagnosis by means of animal inoculation with the blood of suspects fixation of complement with cultures of *T. cruzi* as antigen, intradermal reactions with the culture, and xenodiagnosis are spoken of.

The authors proceed to describe 35 cases in detail with electrocardiograms of each \ ray pictures and line-drawings of the cardiac enlargements in several. In nine of the 26 in which xenodiagnosis was attempted the result was positive. In twelve the intradermal reaction was positive. Five of the 35 died suddenly probably from myocarditis and heart failure. Another died but nothing is known of the mode of death in this case.

H. Harold Scott

- MARTINS A. VERRIANI V & TUPINAMBÁ A. Estudos sobre a Trypanosomíase americana em Minas Gerais Brasil. [American Trypanosomiasis in Minas Gerais.] *Mem Inst Oswaldo Cruz* 1940 July-Sept. v 35 No. 2 285-301 4 graphs & 1 pl. (map)
- PENTO C. Tripanosomíase Cruzii (Doença de Carlos Chagas) no Rio Grande do Sul Brasil. [Chagas's Disease in Rio Grande do Sul Brazil.] *Mem Inst Oswaldo Cruz* 1942 v 37 No 4 443-537 123 figs. on 57 pls [Bibliography]
- VAS E & TORRICO M R A. Estudos preliminares sobre a doença de Chagas na Bolívia. [Preliminary Studies on Chagas's Disease in Bolivia.] *Mem Inst Oswaldo Cruz* 1943 v 38 No 2 165-72 1 pl

LEISHMANIASIS

- SCOVET F G. Kala Azar a Review of its Incidence and Epidemiology in China and Clinical Observations on 585 Cases. Reprinted from *Ann Intern Med* 1944 Oct v 21 No 4 607-27 2 figs. (1 map) [49 refs.]

This article is a good general account of kala azar in China based on published books and papers (49 references are given) and the author's own experience of 585 cases while superintendent of the Bachman Hunter Memorial Hospital Taining Shantung. It was submitted for publication in 1941 but its appearance was delayed because of the author's protracted internment by the Japanese. Since his release the article has been brought up to date by reference to more recent work on the method of transmission and on the occurrence of the disease in the province of Shensi. As regards the various features and characteristics of kala azar in China the article though not been published in the papers quoted, gives no new information which has not been published in the papers quoted. It is of interest however to note that reference is made to published accounts of a disease which must have been kala azar in 1880 and 1888. In fact it is held that the author considers that the incidence of the disease has considerably increased as a result of the disturbances caused by the war. In fact it is held that kala azar owes its prevalence in China to the repeated catastrophes which have ravaged the country between Nanking and Peiping from time immemorial. Many Chinese assert that kala azar follows in the wake of famine flood and war. It is practically unknown in the more tranquil South.

C M Wenjow

- KIRK R. Studies in Leishmaniasis in the Anglo-Egyptian Sudan. VII. Espondia in a Monkey Infected Experimentally with Sudan Kala-Azar. *Trans Roy Soc Trop Med & Hyg* 1945 July v 38 No 6 489-92, 1 fig

Spleen puncture material from a typical case of kala azar in the Sudan was inoculated intraperitoneally to a monkey (*Cercopithecus aethiops*). The animal contracted a fatal infection. Spleen puncture material from this monkey was inoculated to a second monkey. Though infection occurred the animal appeared to make a spontaneous recovery. On two occasions at an interval of about a month spleen puncture material was inoculated intraperitoneally to a third monkey. The monkey remained in good health for over a year when it was noticed it had a small sore on its nose. During the next five weeks this sore extended under a scab till there was extensive ulceration of the nasal and oral region. In the evadate from the sore and in excised tissue leishmaniasis were found. Two shallow ulcers occurred on the tail and another on the middle finger.

of the right hand. In all these lesions as also in puncture material from the spleen, leishmania were found. This is the first time that naso-oral lesions have been noted in experimentally infected monkeys in the Sudan, though many have been studied by the author and others. Occasionally lesions of this type occur in human cases of kala azar and the author has suggested that certain strains of leishmania may be more prone to give rise to them. In the present instance, however there was no evidence that the patient from whom the strain originated had any such lesions.

C. M. Wernon

GRAHAM, J. G. & NAFTALIN, J. M. A Case of Mediterranean Kala-Azar in a British Soldier. *Glasgow Med J.* 1945 July & 26 No. 1 1-7

The infection was contracted in Malta.

PODEB, R., MANGABEIRA, O. Jr. & JANNEY, G. Alguns dados sobre a leishmaniose visceral americana e doença do Chagas no Nordeste Brasileiro (Relatório de uma excursão realizada nos Estados do Ceará, Pernambuco e Bahia) [Kala Azar and Chagas's Disease in North-East Brazil.] *Rev. Inst. Oswaldo Cruz* 1942, v. 37 No. 3 333-67 5 text figs. & 12 figs. on 8 pls. English summary

DE ALMEIDA, E. Um caso de leishmaniose visceral na Paraíba. [A Case of Kala Azar from Paraíba. *B. ant. Medice* 1943 Mar 3 & 10 v. 59 Nos 9 & 10 82-3.

The first case to be reported from Paraíba.

TORRES, C. M. Alterações cutâneas do cão no Kala Azar sul americano. [Skin Changes in Dogs Infected with S. American Kala Azar. *Rev. Inst. Oswaldo Cruz* 1941 v. 36 No. 1 37-67 24 figs. on 12 pls. 17 refs. English abstract.

CHAGAS, A. W. Criação de flebotomos e transmissão experimental da Leishmaniose visceral americana. The Breeding of Sandflies and Experimental Transmission of American Visceral Leishmaniasis. *Rev. Inst. Oswaldo Cruz* 1940 July-Sept., v. 35 No. 2 327-33, 10 figs. on 5 pls.

CHENG, H. L., WANG, C. W. & LEE, C. L. Solustibosan in the Treatment of Kala Azar. *Chinese Med J. Washington* 1944 Jan-Mar., v. 62, No. 1 17-23
[See this Bulletin, 1943, v. 40 229]

CHENG, H. L. & CHOW, H. K. A New Sodium Salt of Mannite Antimonite Acid in the Treatment of Kala-Azar in Chinese Hamsters. *Chinese Med J. Washington* 1944 Jan-Mar. 62, No. 1 28-31
[See this Bulletin 1943, v. 40 229]

CHENG, H. L. Localized Leishmaniasis of the Lymph Glands. With a note by V. T. LIU. *Chinese Med J. Washington* 1944 July-Sept., 62, No. 3 234-92.
This appears to be a report of the case previously described, see this Bulletin, 1943 v. 40 228.

WAR DEPARTMENT TECHNICAL BULLETIN. Wash., D.C. 1945 July 12 pp., 3 figs. Visceral Leishmaniasis—Kala-Azar. [TB Med 183.]

КОЖЕВНИКОВ, П. В. [Cutaneous Leishmaniasis connected with Trauma.] *Med. Parazit. & Parasitic Dis.* Moscow 1944 v. 13 No. 3, 57-9 [In Russian.]

While it is known that traumatic lesions may affect the course and dissemination of cutaneous leishmaniasis, the precise relation between these conditions is not known. The author describes four cases in which it was definitely

established that oriental sore developed on the site of an existing trauma. After considering various possible explanations of this association he concludes that sandflies might have a predilection for injured surfaces of the skin. In support of this view the author mentions that in the course of experimental feeding sandflies were seen to bite those portions of the skin which showed leishmanial infiltration in preference to the intact skin.

C A Hoare

BERBERIAN D A Cutaneous Leishmaniasis (Oriental Sore) V Experimental Canine Cutaneous Leishmaniasis. *Arch Dermat & Syph* 1945 Mar v 51 No 3 193-7 [Numerous refs]

Certain Russian observers working in areas in which human and canine kala azar occur have noted that the disease in dogs is frequently associated with cutaneous ulceration and have rather suggested that purely local lesions in dogs apart from visceral infection, did not occur. On the other hand observers in places where oriental sore alone occurs have seen cutaneous lesions in dogs and have assumed that these correspond to the localized oriental sore of human beings. With a view to throwing light on this question the author inoculated ten pups and one adult dog with cultures of *Leishmania tropica*. The material was inoculated intracutaneously into the skin of the ears or the inner surface of the thighs. In addition some of the dogs were inoculated intraperitoneally. In all animals cutaneous lesions containing leishmania in abundance developed at one or more of the sites of inoculation. In due course when the lesions were well developed and contained numerous leishmania the animals were killed and careful search for leishmania in the viscera made. In no case was it possible to demonstrate a generalized infection. It seems clear therefore that purely local lesions caused by leishmania and corresponding to oriental sore in man do occur. The author while admitting the identity of the parasites in human beings and dogs suggests that the dog strains be named *Leishmania donovani* var *canina* and *L. tropica* var *canina*. [However convenient such a terminology may be it cannot be admitted since the varietal names proposed imply that the canine parasites actually differ from those in man. It would be just as convenient and more correct to write (human strain) and (canine strain) after each name.]

C M Wenyon

FEVERS OF THE TYPHUS GROUP

WOLSTENHOLME B & GEAR J The Serological Diagnosis of Typhus Fever in South Africa. *South African Med J* 1945 May 28 v 19 No 10 162-6

This paper is of interest as showing the help that laboratory workers can expect to obtain from some of the newer methods of serological diagnosis of the louse-borne, flea borne and tick borne typhus fevers.

The authors classify the Weil Felix reactions based on the findings in several hundred cases as follows —

	Louse Typhus	Flea Typhus	Tick Typhus	Mite Typhus
<i>Proctus</i> O\12	++++	+++	++	-
<i>Proctus</i> O\2	+	+	++	-
<i>Proctus</i> O\A	+	+	+	++++

poor resistance to typhus infection and that when on the point of death they are greatly benefited by this vitamin he suggests that *para*-aminobenzoic acid acts in the same way by stimulating cell metabolism, and that drugs with this action are likely to be of value in rickettsial diseases. He has found evidence that they may have an opposite action on diseases caused by the smaller viruses mice suffering from riboflavin deficiency were observed to show increased resistance to poliomyelitis infection

John W D Megaw

SYVERTON J T & THOMAS L. A Method for Staining *Rickettsia orientalis* in Yolk Sac and other Smear Preparations. *Proc Soc Exper Biol & Med* 1945 May v 59 No 1 87-9 1 pl.

The staining methods which give good results with the rickettsiae of epidemic and endemic typhus are less satisfactory for *R orientalis* [*R tsutsugamushi*] in yolk-sac preparations. The authors found that preliminary treatment with lipid solvents enabled good staining to be obtained with Giemsa's stain. Carnoy's fixing fluid (chloroform 3 absolute ethyl alcohol 6 and glacial acetic acid 1 part) was found very satisfactory but other mixtures of chloroform and alcohol also gave good results. Giemsa's stain was prepared by adding 1 cc of concentrated Giemsa's stain (Grübler) and four drops of 0.5 per cent. solution of sodium bicarbonate to 39 cc. of distilled water.

Method—The yolk-sac is washed in normal saline and smear preparations made. The slide is immersed in Carnoy's fluid for 15-30 minutes, dried in air and stained in Giemsa's stain for 15-30 minutes.

Results—The rickettsiae were stained bluish purple. They were mostly extracellular but in some smears a few closely packed rickettsiae were seen within the cells. Smears of peritoneal fluid from mice and hamsters were also stained well by this method.

J F Corson

MONTHLY BULL. MINISTRY OF HEALTH & EMERGENCY PUB HEALTH LAB SERVICE (DIRECTED BY MED RES COUNCIL) 1945 June v 4 122-4 Typhus Fever

This note deals with the prevention of the spread of infection from cases of louse borne typhus fever imported from Europe. Between 21st April and 28th May 1945 11 cases developed in prisoners of war who arrived in England from German camps during the incubation period of the disease which may be as long as 23 days. No lice were found on the patients and no secondary cases occurred.

Between November 1944 and occupation 2 928 cases were reported to S.H.A.E.F. as having occurred in occupied Germany from that time till 4th May 1945 there were 2,874 cases and during the next seven days there were 1 056. Between the middle of April and the middle of May over 83 foci of the disease were reported from the area covered by S.H.A.E.F.

The precautions needed in connexion with sporadic imported cases are described. A summary of these is as follows—

(1) *Expectancy*—The possibility that attacks of fever among recent arrivals from suspected areas may be due to typhus should be borne in mind even when another diagnosis such as pneumonia seems justified. One of the diagnostic features specially mentioned is the appearance of the characteristic macular rash *never involving the face on the fourth or fifth day*. [This statement must be read with care. If the absence of a comma after the words in italics is not noted it might wrongly be assumed that the rash never extends to the face.]

It is pointed out that although few cases are likely to be imported, an attitude of expectancy on the part of practitioners forms the first line of defence.

(2) *Delousing*—This will usually have been carried out before arrival in this country but in all cases of doubt it ought to be repeated. A powder containing 5 per cent. of DDT (A.L. 63 Mark III) and a suitable blower can be obtained from the P.R.M.O. of the Ministry of Health. A horticultural blower or sugar dredger can also be used. For each person an average of 1½–2 oz. of the powder is needed. This is blown inside the hat, up the sleeves (with the arms extended laterally) down the back and front of the trunk through the neck band and through the waistband all over the parts below the waist. The powder must be blown between the layers of clothing and between the inner layer and the skin so as to ensure impregnation of every part of the clothes with the dust.

If no blower is available the clothing is removed, dusted with the powder and placed in a pile to which several hard blows are given.

The powder will kill invading lice for 2–4 weeks but it does not kill nits so that 1–2 teaspoonfuls of lethane hair-oil are applied to the hair.

(3) *Immunization*—This is specially intended for persons employed on typhus control or who are otherwise exposed to particular risk. The vaccine, with instructions for use may be obtained from the Medical Research Council c/o London School of Hygiene and Tropical Medicine Keppel St. London, W.C.1 or from the Emergency Public Health Laboratories. Any reactions that occur are usually mild, especially in cases of revaccination. Immunity is fully developed in about four weeks; the vaccine does not provide a guarantee against attack, but greatly modifies their severity. *John W. D. Meager*

BEACH, H. L. W. & RENNIE, J. H. Four Cases of Typhus Fever in Great Britain.
Brit Med J 1945 Aug 4 153–4 1 fig

These four cases occurred among war prisoners who had returned from a camp in Germany. They had been disinfested with DDT powder two days before reaching England and on arrival they were found free from lice. The periods elapsing between disinfection and onset were 7, 9, 11 and 27 days. Three of the patients had been under observation in the hospital since their return so the whole course of the illness was observed. The Weil-Felix titre rose to 1–1,000 in every case.

One of the patients, a man of 44 years, died on the 14th day—a septic finger had to be incised on the 2nd day of his illness. Two other patients had fairly mild attacks lasting about a fortnight. The fourth patient, aged 29, had an exceedingly mild attack; his temperature rose to 103.2°F within 12 hours of the onset. It remained high for two days, then became low intermittent in type; the whole attack lasted six days and the patient's condition was excellent even while the temperature was high. No rash was seen. The onset in this case was 27 days after disinfection; this interval was longer than the generally accepted maximum incubation period of 23 days. It was suspected that there had been contact with the patient first attacked though no other secondary cases occurred. The Weil-Felix titre on the 2nd day was 1–50; on the 6th day it was 1–1,000.

In view of the mildness of the attack the question of previous immunization arose but the patient did not know the nature of the last vaccine he had received nearly two years earlier.

The clinical picture in the other three cases conformed to that of one or other of the recognized types of typhus fever except that the temperature showed a pronounced tendency to be remittent or intermittent. From the charts illustrating the paper it is seen that the temperature of one patient fell to normal on the 3rd, 4th, 9th, 10th and 13th days.

Penicillin was administered to all the patients with the object of preventing secondary infections; the dosage was 15,000 units by intramuscular injection

every three hours but the first injection was not given before the 10th day except in the mildest case in which it was given on the 2nd day the duration of the treatment is not stated and the authors disclaim any attempt to draw any conclusions on its effect

[The source of infection in the very mild case is likely to remain an unsolved mystery though it is possible that infected louse faeces may have been deposited on some article of the patient's clothing before disinfection was carried out. Typhus rickettsiae are known to remain virulent for long periods in dry insect droppings and it is believed that persons who handle infected clothing may acquire the disease either by inhaling infected dust or by direct contact. Disinfection would not prevent the occurrence of this kind of infection and some experts insist on the necessity for disinfection of the clothing and body of any person who is likely to harbour infected lice. Thorough disinfection is often impracticable in the presence of an epidemic but it offers the only guarantee of eliminating the risk of persistent infection.] *John H. D. Megaw*

HUSSAIN, N. Typhus in Kashmir. *Indian Med Gaz* 1945 Mar v 80 No 3 132-3

In the main valley of Kashmir at altitudes ranging from 5 000 to 12 000 feet outbreaks of typhus fever have been reported from time to time. The epidemics briefly described in the present paper occurred in the winters of 1942-43 and 1943-44. The persons chiefly affected were members of a cattle-keeping community who spent the winter seasons in crowded insanitary conditions and who were heavily infested with lice. In 1942-43 1 526 cases were reported of which 408 were fatal. In the following winter there were 946 cases with 320 deaths mostly in one district. Probably there were many more cases.

Protective immunization by vaccine was used on a small scale apparently with good results. *John H. D. Megaw*

JACKSON, D. S. Typhus Fever in Gilgit. *Indian Med Gaz* 1945 Apr v 80 No 4 207-8.

The author records his impressions based on 213 cases only five of which were fatal. Treated by him in the hospital of the Agency Headquarters Station of Gilgit (altitude about 5 000 feet in Kashmir) between November 1943 and August 1944. 139 of the cases occurred during the four months February-June. In August there were only four cases.

Most of the patients belonged to the poorer classes. There was evidence of transmission from person to person. The doctor in charge of the medical ward and two members of the hospital staff were attacked.

A typical rash appeared between the 5th and the 7th day in every case. There was delirium in 80 per cent. of the patients. The onset of this coincided with the appearance of the rash.

The infection was [quite naturally] regarded as louse-borne.

John H. D. Megaw

VARELA, G. & ZOZAYA, J. Distribución en México de las cepas de tifo exantemático hasta ahora estudiadas. [Distribution in Mexico of the Strains of Typhus so far Studied.] *Rev Inst Salubridad y Enfermedades Trop* Mexico, 1945 Mar v 6 No. 1 11-14 1 fig. English summary (4 lines)

GENTSCHOFF P. Z. Farbege Agglutination zur Schnell-diagnose des Fleckfiebers. [Slide Agglutination of Stained *Proteus* as a Rapid Test for Typhus.] *Zent f Bakt I. Abt. Orig.* 1944 Mar 10 v 151 No. 4/5 261-3

The rapid slide-agglutination test described by the author differs in no essential respect from the one introduced by BRUMPT in 1940 [see this *Bulletin* 1945 v 42, 197]. Reference is made to five slide tests but all these are of German origin.

The author attaches importance to the use of a special synthetic medium for the preparation of the *Proteus* cultures used in making the suspension, he uses a mixture of malachite green and pararosanilin for staining the bacilli, and he stores the suspensions in a patent drop-bottle. Those interested in details of the technique must consult the original article.

John W. D. Megaw

DONOVICK, R. & WYCKOFF R. W. G. The Comparative Potencies of several Typhus Vaccines. *Pub Health Rep Wash* 1945 June 1 v 60 No 22, 605-12.

This paper was approved for publication on October 22nd, 1942, but was withheld because of the subject matter. It describes the results of an investigation carried out in continuation of the experiments previously reported (see this *Bulletin* 1945 v 42, 792). It is now stated that the vaccine labelled IIA was treated by ether after centrifugation, and the one labelled IIIA was refined by TORRINO's method in which the crude vaccine was extracted with ether. Another series of vaccines prepared by the same methods and labelled TIA, TIIA and TIIIA were tested, with the same results.

Other experiments were carried out with the vaccines. By these it was found that the complement fixation titre in guinea-pigs treated by single doses of the vaccines reached its maximum in about four weeks. And that after small single doses of weak vaccines the titre was low and soon fell to an insignificant level, whereas with potent vaccines the titre rose to a great height and took many weeks to fall below a measurable height.

Alum precipitation of the vaccines did not enhance the titre of the reaction and caused no delay in its fall.

John W. D. Megaw

DE VIDAS J. A Survey of Scrub Typhus (K Typhus) in New Guinea. *Med. J Australia* 1945 June 23 v 1 No 25 631-4 6 figs.

The author's description of the clinical and pathological features of "scrub (mite-borne or K) typhus" is based on a study of 80 cases of which 20 were fatal. [This exceptionally high fatality rate in a group of patients whose average age was 26 shows that the infection must have been very virulent. Presumably also the patients had been debilitated by hardship.]

The infected areas were patchy. They comprised open prairies of kumai grass, rain forest, areas, untended plantations and jungle growth. Wet humus for the larval mites, and available food for the rats were conditions essential for the maintenance of infection in a locality.

D. C. SWAN is quoted as stating that in the Goodenough Island the mites of the scrub-typhus areas belong to different species from those in the nearby "scrub-itch" areas. The consensus of opinion was that *Trombicula fleckleri* and *Tr. australis* transmit scrub typhus while *Tr. mediocres*, *Schöngastia pusilla* and *Sch. blestoid* cause scrub itch.

A description is given of the clinical and pathological features of two fatal cases in which death occurred after illnesses lasting 12 and 13 days, respectively.

Among 15 cases in which a post-mortem examination was made an ecarh occurred in 11, a rash in 11, and adenopathy and splenomegaly in all. Other

features were severe myocarditis in nine cases less severe myocarditis in 6; bronchopneumonia in 7 cloudy swelling and congestion of the kidneys and liver in all the 15 cases severe congestion and oedema of the lungs in 8 hydrothorax in 7 haemorrhages in the mucosa of the pelvis of the kidneys in 3 and petechial haemorrhages in the meninges in 3

The predominant histological lesion was a perivascular infiltration by lymphocytes and histiocytes especially in the lungs heart liver kidneys spleen and lymph glands. Swelling of the vascular endothelium with a tendency to thrombus formation as described by CORBETT was not usual though in specimens from two cases not belonging to this series vasculitis and endothelial proliferation with thrombosis and haemorrhage were pronounced in addition to perivascularitis both of these patients died after an illness of about six weeks.

The author suggests that in scrub typhus the inflammatory process spreads from the outside of the vessels towards the interior whereas in classical typhus it spreads centrifugally from the endothelium. [This view is not supported by the descriptions given by other observers of the microscopic changes in the two diseases.]

The average Weil-Felix response for *Proteus OAK* was—a titre of 1-160 on the 10th day rising to the maximum height by the 22nd-25th day beginning to decline 5-7 days later and finally disappearing in two months. Titres below 1-160 were not regarded as significant [but FELIX attaches great importance to low titre reactions when an earlier test has been negative]

The author obtained good results with a rapid slide agglutination test based on the modification of the Kudicke and Steuer test described by BARDHAN *et al* [this *Bulletin* 1944 v 41 379] On a drop of dried blood two drops of concentrated *OAK* suspension are placed after a minute the slide is gently rocked for 5-10 minutes White granules appear when the reaction is positive

SINGH G Report on an Epidemic of Scrub Typhus (K Form) treated at a General Hospital in Burma. *Indian Med Gaz* 1945 Apr v 80 No 4 189-201

Within 24 days in September 1941 107 cases of scrub typhus were seen at a general hospital in Burma all but two of the patients belonged to one unit which was camped in a rural area. Only two of the patients died In 88 cases there was enlargement of the lymph glands either generalized or associated with a necrotic patch situated on the chest or shoulders in 19 on the trunk in 11 and on other parts of the body in 8 A rash appeared between the 3rd and 5th day in 38 cases it was macular in 30 and papular in 8. In 42 cases the leucocyte count was 9 000-13 500 per c.mm. in 12 it was less than 5 000 per c.mm.

The Weil-Felix reaction was of the *OAK* type in all cases except for three of these in which the titre was 1-80 or 1-160 the range of the maximum titre was 1-320 to 1-10,240 In 1-6 cases *OAK* and in all 11 cases *O12* were also agglutinated at titres ranging from 1-40 to 1-320

In 10 cases there was an after fever regarded as a relapse after falling to normal the temperature rose again 1-5 days later and fever of an intermittent or continued type lasting 4-5 days occurred.

The author makes the following statements—The rat flea *X. cheopis* has been implicated in the transmission of scrub typhus and ticks in other forms and. There is reason to suppose that in this outbreak of scrub typhus the disease normally sporadic achieved epidemic proportions owing to the change of vector i.e. conveyance by lice within a louse-infested unit.

[These statements are surprising: perhaps the article was written before it became generally known that mite-borne typhus can occur in the form of sharp epidemics when bodies of troops enter infected areas. The reviewer's earlier classification of the typhus fevers as epidemic and "non-epidemic" may have been responsible for misunderstandings in this connexion: his later classification of the fevers as demic and zootic was proposed for the purpose of avoiding ambiguity (see *Brit Med J.*, 1942 Oct. 10 433).

Epidemic typhus often occurs in endemic or sporadic form, and fevers that primarily affect lower animals may occur in epidemic form: hence the desirability of adopting the rarely used words demic and zootic for primarily human and primarily lower animal diseases.

John W. D. Magee

MENON M. C. & ISBORSON C. Scrub Typhus: a Clinical Study. *Brit Med J.* 1945 Jul 28 112 14

In the last two months of 1944 and the first month of 1945 there were 110 cases of scrub typhus among the soldiers of a British unit which had entered a small typhus island in North East Burma.

The onset was usually sudden: all the patients had severe headache with frontal or post-orbital localization: the temperature reached its maximum within 48 hours after which the fever was continued, though in some cases there were occasional intermissions with profuse sweating: the termination was by lysis.

Some of the other features were as follows (the figures in brackets show percentage incidences):—Early sore throat (54) occasionally with dysphagia (3.6); eschar (56) in two cases there were two eschars and in one case there were three; conjunctival injection (82) and flushing of the face (65) appeared about the 3rd day: a moderate degree of generalized enlargement of the lymph nodes (83) could be detected from the 4th day: the rash (64) usually maculopapular but occasionally purely macular appeared on the 5th or 6th day and lasted 3-4 days: it was mainly on the trunk, face, upper arms and thighs.

The mental changes (50) in average cases were apathy and confusion, in severe attacks there was restlessness, delirium, or a typhoid state. Diffuse bronchitis (50) with mucoid sputum occasionally blood tinged was regarded as part of the syndrome: but when the sputum was purulent or the leucocyte count over 10,000 per cmm extraneous infection was believed to be the cause. Cyanosis was a danger signal: haecup (20) was distressing when it occurred, it was a feature of six of the nine fatal cases. A progressive fall in the blood pressure occurred in patients who were going downhill. Nerve deafness was common. Neck rigidity (3-4) was not associated with any change in the cerebrospinal fluid. Blood counts were seldom abnormal.

The titre of agglutination of *Protein OVA* was less than 1-125 in 20 undoubted cases.

Bronchopneumonia or lobar pneumonia occurred in seven cases: in three of these empyema followed in spite of treatment by sulphathiazole: repeated aspiration, together with local and general treatment by penicillin had to be carried out: in one of these cases penicillin failed because of a secondary infection with *Bact. coli* and resection of a rib was needed. Other complications were—parotitis in one case, femoral thrombosis in two cases, mild peripheral neuritis in six cases and bedsores in three. Coexistent malaria occurred in 15 patients: two of whom had cerebral symptoms. Nine patients died, one suddenly of myocardial failure on the 4th day of convalescence and another as a result of haematemesis: in the latter case numerous small haemorrhages were found after death in the stomach and intestine: the remaining seven deaths were attributed to toxæmia, they occurred between the 12th

and the 24th days. In some of the bodies subpleural haemorrhages were found.

Treatment was by an adequate diet containing at least 2,400 calories and 100 gm. first-class protein and by combating dehydration and salt depletion. In some cases a transnasal tube was used. Patients were kept in bed till the pulse rate became normal usually for 10-13 days after defervescence. Hiccup responded temporarily to inhalations of CO_2 and oxygen. Cyanosis was treated by oxygen which had to be continued for three days in some cases. Malaria was so common that a therapeutic course of mepacrine was given at the onset in all cases. This was followed by suppressive treatment. *John W D Megaw*

SATHER R O & SILBERSTEIN J S. Scrub Typhus. *Bull U S Army Med Dept* 1945 July v 4 No 1 68-75 1 chart

This paper deals with 14 sporadic cases of scrub typhus which occurred in the four months August to November in New Guinea. The onset was insidious with severe fronto-parietal headache. Weakness and apathy were very pronounced during the early stages. An eschar was seen in only one case. A rash was seen in four cases. It was maculo-papular in two, macular in one and scarlatiniform on the abdomen in one. Local or generalized lymphadenitis occurred in four cases and four patients had subconjunctival haemorrhage. The fever was remittent in all the cases. The temperature fell to normal by lysis on the 13th-15th day.

The *Proteus* OXA titre was determined on several occasions in most of the cases. Of four sera tested towards the end of the 1st week, two were negative and the titres in the other two were 1-40 and 1-80. 11 sera tested towards the end of the 2nd week gave the following titres: —0 in three, 1-40 in two, 1-80 in four, 1-160 in one and 1-320 in one. The titres in 12 cases tested from the 21st to the 25th day were: —1-40 in one, 1-160 in four, 1-320 in one and 1-640 to 1-2,560 in the rest. In one case the titre never exceeded 1-80 which was reached on the 14th day. Negative reactions having occurred on the 7th and 12th days.

There were no deaths but some of the patients developed a picture of shock and were treated with good results by plasma in doses of 100-200 cc.

In a description of two cases it is stated that 3,500-4,000 cc. of fluid were given daily by oral and parenteral routes.

The protean nature of the disease is stressed. *John W D Megaw*

GOTTFRIED S P. A Preliminary Study of Blood Chemistry Findings in Scrub Typhus. *Amer J Clin Path* 1945 Feb v 15 No 2 71-8. [14 refs.]

In view of the lack of information on the blood chemistry of scrub typhus the author has made this comprehensive investigation.

Between November 1943 and February 1944 47 patients were studied as far as possible at three stages of the disease: these stages were during the 1st week, at the height of the fever, and just after defervescence. Healthy controls who had never suffered from scrub typhus, syphilis or jaundice were investigated simultaneously. The procedures adopted are described or named. The table below has been compiled from the detailed tables contained in the paper.

Blood sugar values were practically normal. Blood urea nitrogen was high in one fatal case. The lowering of the plasma carbon dioxide in 11 patients in the 2nd stage was not regarded as important; it was attributed to tachypnoea. The fall in the plasma chlorides is an indication for chloride therapy. The low serum protein may have resulted from exhaustion and malnutrition rather than from infection; most of the patients had come from combat areas. The persistence of low serum albumin in early convalescence shows that the rise in the

	Stage I	Stage II	Stage III	Controls
Plasma carbon dioxide				
Subnormal	0	11	1	0
Normal	16	30	33	25
Plasma chlorides				
Subnormal	8	29	2	2
Normal or high	8	19	32	23
Serum proteins				
Subnormal	8	18	2	2
Normal or high	10	23	37	23
Serum albumin				
Subnormal	10	33	25	1
Normal	8	8	9	24
Albumin-Globulin ratio				
0.5-0.9	1	4	8	0
1.0-1.4	3	21	16	0
Normal	11	16	12	25

Also one in which it was 3.1-3.5.

total serum proteins during the fever was due to an increase in the globulin and this may have been associated with stimulation of the protective mechanism of the body. Plasma fibrinogen was low in 40 per cent. of the cases but also in 20 per cent. of the normal controls so that environmental factors must have contributed to the fall. In some cases the icterus index and the urobilinogen content were high, but the same features were found in controls who were taking atabrin. Liver function tests with bromosulphalein gave practically normal results. Serum calcium was normal in the 20 cases in which it was estimated.

John W. D. Meigs

LUCAS R. B. Isolation of a Strain of *Rickettsia orientalis* from Cases of XK Typhus in Ceylon. *Indian J. Med. Res.* 1944 Oct., v. 32, No. 2, 223-8. [13 refs.]

This paper is of special interest to workers concerned with the isolation of rickettsiae in cases of scrub typhus and other fevers of the typhus group. The author mentions the great range of variability observed in the reaction of guinea pigs to intraperitoneal injections of blood from patients suffering from "XK typhus." With many strains of infection it has been impossible to isolate rickettsiae or even to detect any febrile reaction with a few strains repeated passages have been made and there has been a consistently high mortality among the guinea pigs.

In the present experiments 12 guinea pigs and three white rats were inoculated with pooled suspensions of blood clot from groups of patients between the 7th and 14th days of their attacks of scrub typhus. Blood from 14 patients was employed. In one of the white rats enlargement of the spleen was found after the death of the animal on the 19th day otherwise no significant reaction febrile or of other type was detected in any of the animals. Despite the absence of apparent reactions three separate series of passages through guinea pigs were undertaken, pooled brain and spleen substance obtained on the 12th to the 14th day being used for each passage. The original inoculum used in the first series of passages was obtained from a guinea pig inoculated with pooled clot from two patients on the 12th day. In the other two series it was from two white rats inoculated with pooled clot from three patients on the 14th day. Brain and spleen material from the last guinea pigs employed in the above

series of passages was then pooled and inoculated into two guineapigs from which 14 days later a pooled suspension of brain and spleen substance was prepared and injected intraperitoneally into two white mice both of which died one after 17 days the other after 18 days.

Although no guineapig inoculated in the three series each of which comprised four passages showed any apparent reaction the white mice developed an abundant exudate in the peritoneal cavity and smears made from this contained numerous *R. orientalis* located in the endothelial cells.

The infection must have been transmitted through the guineapigs and white rats in inapparent form and the white mouse is considered to be the experimental animal of choice for this type of work.

A suspension of blood clot from four 12th day patients was injected into the anterior chamber of the eye of four rabbits no reaction followed in these animals or in others inoculated in the same way with suspensions of lymph glands removed at biopsy from patients on the 24th day.

Attempts to infect the yolk sac of ten embryo chicks with blood-clot material from patients also failed.

John W D Megaw

LEWTHWAITE R. Scrub Typhus. [Correspondence] *Lancet* 1945 June 16 770

Lewthwaite remarks that in one theatre of war in the Far East scrub typhus is probably by now the only disease that kills men in more than trivial numbers. He notes that scrub-itch has rarely been seen in the troops and has seldom if ever been associated with the occurrence of scrub typhus. In fact the opinion is widely held that the two conditions are caused by separate species of mites. Lewthwaite goes on to refute a statement that scrub typhus was at one time thought to be tick borne, and to quote some of the evidence by which transmission by larval mites has been proved.

Charles Wilcocks

RODHAIN J & BARLOVATZ A. L'histologie de l'escarre dans la fièvre pseudo-boutonneuse de la région du Maniema (Congo Belge) [The Histology of the Eschar in the "Fievre Pseudoboutonneuse" of the Maniema Region (Belgian Congo)] *Ann Soc Belgs de Méd Trop* 1944 June 30 v 24 Nos. 1-2, 37-42 4 figs. on 2 pls.

The authors describe the histology of an eschar excised from the scrotum of a patient on the 7th day of an attack of a fever called the pseudo-boutonneuse or pseudo-typhus fever of Maniema. [The latter name is unsuitable in two respects. It suggests that the fever is the same as the pseudo-typhus described by SCHUFFNER about the year 1909 and now known to be mite-borne typhus also even if the fever were the same its name ought to be translated into French as pseudo-typhoïde. Schuffner himself translated it into English as pseudo-typhoid.]

The loss of tissue in the lesion was limited to the epidermis. The vascular and perivascular lesions in the dermis were similar to those described in the papular eruptions of typhus fever. The eschar is said to differ from that of boutonneuse fever and tsutsugamushi disease in the absence of any evidence of an infecting bite and in the restriction of the necrotic process to the epidermis and the superficial layer of the dermis. The authors state that these differences may suggest the occurrence of infection by deposition of infected material on the surface of the skin rather than by injection through a bite.

John W D Megaw

HARRELL, G. T. WOLFF, W. A. & YEANING, W. A New Approach to Basic Supportive Therapy in Rocky Mountain Spotted Fever. *Southern Med. J.* 1945 June v. 38 No. 6 367-70 1 fig.

This paper is of wider interest than the title suggests: the general treatment of Rocky Mountain spotted fever can safely be assumed to follow the same lines as are suitable for the other typhus fevers.

The author states that the pathologic physiology of the disease is quite comparable with that of extensive burns: in both of these conditions there is leakage of proteins through the walls of the blood vessels into the tissues; treatment by salines and glucose causes a further escape of the proteins and prevents their reabsorption with the result that oedema develops and a further fall occurs in the blood pressure. Transfusions of plasma, on the other hand, promote the reabsorption of crystalloids into the vessels. The treatment of a number of very severe cases of Rocky Mountain spotted fever was carried out in accordance with this principle: as much as 2,500 cc. of plasma was given within 36 hours to a boy aged 15 years.

The treatment was controlled by frequent estimations of the non-protein nitrogen, the chlorides, and the total serum proteins of the blood.

The authors mention the studies of WOODWARD and BLAND in which a favourable reference is made to the use of plasma in some cases of epidemic typhus fever [this *Bulletin* 1945 v. 42, 189].

In discussing the paper V. H. TORRING pointed out that the patients had come under treatment at a late stage and that some of the changes described would not have occurred if adequate fluids and a high protein diet had been given from the onset: he also advised great caution in carrying out the recommendations because of the danger that was involved.

John W. D. Meyer

ANIGSTEIN, L. & BADER, M. N. Para-Aminobenzoic Acid—its Effectiveness in Spotted Fever in Guinea Pigs. *Science* 1945 June 8, 591-2. Also in *Texas Reports on Biol. and Med.* 1945 3 No. 2 253-4.

Experiments are described showing the effect of PABA (para-aminobenzoic acid) on guinea-pigs infected with a virulent strain of Rocky Mountain spotted fever which killed 100 per cent. of untreated control animals. The guinea-pigs were fed *ad lib.* on a high-protein diet containing 2 gm. PABA per 1.00 gm.

The drug was started 24 hours before the infecting inoculation in 12 guinea-pigs: seven of these remained completely afebrile; five had fever lasting 1-3 days; there were two deaths.

Among 17 guinea-pigs whose treatment started on the day of inoculation, 11 remained afebrile, three had fever lasting 1-2 days, two had typical fatal attacks and one died without fever.

When the drug was given for the first time during the incubation period—in some cases as late as 72 hours after inoculation—50 per cent. of the animals remained afebrile, in spite of the fact that their appetite was capricious so that smaller doses of the drug were taken.

The action of PABA appeared to be purely suppressive: spleen substance of the treated animals, when inoculated into normal guinea-pigs, caused typical fatal attacks.

John W. D. Meyer

BARTONELLOSIS

SAMANIEGO B M Comisión de estudios sobre bartonellosis Pasto-Nariño-Colombia. Situación actual y programa [Commission for the Study of Bartonellosis. Present Position and Programme for the Future.] *Rev Facul de Med* Bogotá, 1944 Nov v 13 No 5 523-30 English summary

In 1936 a peculiar disease appeared in Southern Colombia with a high mortality rate about 1 per cent of the total population. Various diagnoses were proposed—typhoid fever pernicious malaria, yellow fever brucellosis trypanosomiasis—before PATIÑO CAMARGO in 1939 showed that the condition was a form of bartonellosis [see this *Bulletin* 1940 v 37 271 582 583 1941 v 38 209 1943 v 40 904] and it was found to be more extensive than had been believed and its appearance was recorded in Ecuador Peru and Guatemala. The disease was originally known as Guaitara fever and the vector proved to be *Phlebotomus*. In Colombia the districts affected were the Departments of Nariño and Cauca and mainly the valleys of the rivers Pacual Guátara Juanambá Mayo and Sambingo tributaries of the Rio Patía.

The National Government in 1939 instituted a campaign against bartonellosis. At first its efforts were confined to helping the victims by establishing hospitals in the chief foci later attention was given to raising the standard of living of the poorer inhabitants who were the main sufferers from the disease. In successive years from 1940 to 1943 the total cases in Colombia were 571 486 750 and 434 with deaths numbering 142 (fatality rate 24.8 per cent) 104 (21.4) 99 (13.2) and 24 (5.5) respectively.

The total population of the bartonellosis zones is stated to be 180 000 and the morbidity rate is very high 24 per cent in ordinary times higher of course in epidemics. The chief causes of death are tuberculosis malaria typhoid and typhus fevers malnutrition and intestinal parasitism. The author examined 100 persons [he does not say how they were chosen] and found 25 so ill that they could do no work at all 70 in poor health anaemic undernourished and paratized, but able to work only five out of the hundred were enjoying good health.

The programme of the Health Authorities for the future comprises in addition to study of the epidemiology of and research on bartonellosis, widespread anti-malaria drainage erection of large numbers of dwellings with proper and adequate sanitation delousing to prevent the spread of typhus and propaganda and education in health matters.

H Harold Scott

KESSLER W R. & ZWEMER, R L. Studies on Experimental *Bartonella* Anemia in the Albino Rat. III. Potassium and other Blood Changes. *J Infect Dis* 1944 Sept-Oct v 75 No 2 134-7 1 fig

During acute infection with *Bartonella muris* in the adult rat there is a terminal increase in the plasma potassium level which occurs immediately before death. This may be a result of the red cell destruction. There is also an increase in the clotting time of blood of infected rats.

CARR D T & ESSEX H E. Bartonellosis a Cause of Severe Anemia in Splenectomized Dogs. *Proc Soc Exper Biol & Med* 1944 Oct v 57 No 1 44-5 1 fig

After splenectomy had been performed on a dog severe anemia developed and stained smears of the blood revealed organisms that had the morphologic characteristics of *Bartonella canis*. The disease was transmitted to two other dogs confirming the diagnosis of bartonellosis.

YELLOW FEVER

EPIDEMIOLOGICAL INFORMATION BULL. (UNRRA HEALTH DIVISION)
WASHINGTON D.C. 1945 June 15 v. 1 No. 9 363-70 Standards for
the Manufacture and Control of Yellow Fever Vaccine.

Certain requirements for the preparation, preservation and use of yellow fever vaccine have been adopted by the U.N. R.R.A. Expert Commission on Quarantine

An aqueous base (serum-free) type of vaccine is to be prepared according to methods described [thus *Bulletin* 1943 v. 40 692 1944 v. 41 123] the dried product must contain not more than 1 per cent of moisture and it is sealed in glass ampoules filled with nitrogen. The 17D strain virus of the 200-300th subculture [*ibid* 1937 v. 34 690] is used and must conform to certain requirements on testing in monkeys [*ibid* 1944 v. 41 125 1945 v. 42, 803]. In the monkey safety test on the secondary seed virus the serum of inoculated monkeys (*Macaca mulatta*) must show a certain standard of virulence to mice and at least five out of the six inoculated monkeys must become immune not more than two of the six monkeys may develop encephalitis. Chick embryos from virus-inoculated eggs should preferably be not over 11 days old [*ibid* 1942, v. 39 689]

The finished vaccine when rehydrated to its original volume shall contain not less than 150 000 M.L.D. (L.D.₅₀ for mice) at least 500 M.L.D. should be used to vaccinate man. Random samples of the finished vaccine must be tested on guinea-pigs 4-5 cc. being injected intraperitoneally no significant clinical reaction shall occur but if a reaction does occur in one of two guinea-pigs, a re test is made on three and not more than one shall show a reaction. Random samples are also tested for sterility

The labels shall show certain details. The "date of manufacture" is the time of passing a satisfactory potency test the "date of issue" is when distribution begins and must not be later than one year after the date of manufacture the expiration date must be not more than one year after the date of issue. Certain temperatures at which the virus must be kept are specified.

For use the vaccine is diluted 1:10 in normal saline and 0.5 cc. is immediately injected subcutaneously the dose is the same for children and adults. Other regulations relate to shipping and the official release of the vaccine.

The seed virus must be preserved in the dry state under nitrogen at -70°C. or colder. If properly prepared and stored it will remain viable for an indefinite number of years. The secondary seed virus is prepared as chicken embryo pulp similarly to the preparation of the pulp for vaccine production and is stored in ampoules like the primary seed virus.

J. F. Corson

SPRAGUE H. B. & BARNARD J. H. Egg Allergy Significance in Typhus and Yellow Fever Immunization. *U.S. Nat. Med. Bull.* 1945 July v. 45 No. 1 71-4

Reactions after inoculation occurred in two men who were sensitive to egg protein in one the inoculation was with yellow fever vaccine prepared from chick embryos, while in the other it was with typhus vaccine made by the Cox yolk-sac method

The first patient, aged 20 was admitted to hospital for examination because he had developed severe asthma within 15 minutes after receiving the first dose of yellow fever vaccine five months before he also showed oedema of the face and generalized urticaria at the same time

As a child he had suffered from eczema up to 2 years of age and from asthma up to 8 years of age he had long been sensitive to white of egg and to various

nuts and tests about the time of his admission showed a sensitivity to ragweed pollen egg white house dust horse serum cotton seed cow dandruff flax seed chicken meat typhus vaccine 1 10 and yellow fever vaccine 1 10. Mouse protection tests showed that he had developed immunity to yellow fever in spite of his reaction.

The second patient aged 23 had been vaccinated simultaneously with typhus vaccine a typhoid booster shot and 0.5 cc of tetanus toxoid. Within two hours he developed massive generalized oedema, dyspnoea, dysphagia and coryza. Eggs had always caused angioneurotic oedema of his mouth and throat and swelling of his neck glands and in 1935 he had had an almost fatal reaction to horse serum in tetanus antitoxin. As a child he had suffered from eczema and later from hay fever. Tests showed sensitivity to typhus vaccine tetanus toxoid yellow fever vaccine egg white horse serum but not to triple typhoid vaccine. A year before he had had no reaction to tetanus toxoid and yellow fever vaccine.

The authors think that such persons should be excluded from the Services.

J. F. Corson

DENGUE

SABIN A. B. & SCHLESINGER R. W. Production of Immunity to Dengue with Virus modified by Propagation in Mice. *Science* 1945 June 22 640-42.

Most of the interesting experiments described in this paper were carried out with an exceptionally virulent strain of dengue virus isolated during an outbreak in Hawaii. The serum of persons infected with this virus contained 1 000 000 infecting doses per cc. and by ultracentrifugation a concentrate was obtained containing 10 times this number of infecting doses. Repeated attempts to transmit the concentrated virus by passage through embryo chicks and the first two attempts at passage through mice by intracerebral inoculation resulted in failure but eventually the authors succeeded in effecting a series of 16 passages up to the date of writing by intracerebral inoculation of 10- to 12-day-old albino Swiss mice. Only 10-20 per cent of the originally inoculated mice showed signs of infection and the incubation period was often 3-4 weeks but with passage through the mice a progressively increasing number of the animals showed nervous-system manifestations and the incubation period became shorter it was about two weeks at the 6th passage. At the 14th passage 90 per cent of 20 three-weeks-old mice showed signs of infection but only one of 10 six weeks-old mice of the same strain was affected, and very few reactions occurred among some other strains of albino Swiss mice. Cotton rats guinea-pigs hamsters and rabbits gave no reactions to passage strains. It was found later that although unconcentrated infected serum of human origin failed to infect mice the same serum diluted 1-100 was infective this suggested the presence of an inhibitor in the serum.

Among four strains of dengue virus isolated in New Guinea only one was capable of infecting mice and this strain had been found by the senior author to be immunologically identical with the Hawaiian strain whereas the other three showed some degree of immunological difference.

Small doses of suspensions of the brain and spinal cord of infected mice up to the 6th passage caused dengue sometimes moderately severe when injected into volunteers. Material from the later passages sometimes caused no fever sometimes there was a brief febrile reaction on the 8th 9th or 10th day the usual response was an extensive maculo-papular rash and the occurrence of petechiae on the feet. The senior author (unpublished) had previously

observed "an interference phenomenon between yellow fever vaccine and the regular unmodified dengue virus in human beings" so he added yellow fever vaccine to the virus with the interesting result that only a faint rash and no petechiae appeared in inoculated persons. All the nine volunteers inoculated with virus of the 7th 8th or 10th passage became immune to dengue as was shown by negative responses to bites by mosquitoes of proved infectivity. Volunteers inoculated with a mixture of yellow fever vaccine and dengue virus were examined later by Dr. Max THEILER and found to have neutralizing antibodies for yellow fever also.

Aedes aegypti mosquitoes became infective after feeding on volunteers at the time of the appearance of the rash resulting from inoculation with the virus of the 7th and later passages. Large numbers of the mosquitoes had to be used and the intrinsic incubation period in the insects was prolonged to more than three weeks. The reactions caused in persons who were bitten by these infected mosquitoes were atypical; the evidence of infection consisted in the rash and the typical leucocyte changes.

The immunity produced by the dengue vaccine is not likely to be more lasting than that resulting from an attack of the disease, but the vaccine might be of considerable value in special circumstances.

It would perhaps be too much to expect that the modified virus would be capable of maintaining the mosquito-man-mosquito cycle for a prolonged period without loss of infectivity or increase in virulence. If this happened it would be possible to protect a community against severe outbreaks of dengue by releasing a number of mosquitoes infected with the modified virus. The enlistment of the local mosquitoes as unpaid vaccinators would be an inexpensive method of control, if it worked, but mosquito control, facilitated by DDT is likely to remain the most satisfactory method of prevention.

John H. D. Meyer

PLAGUE

DE VILLAFANE LASTRA, I. El sulfathiazol en el tratamiento de la peste de Oriente. [Sulphathiazole in the Treatment of Plague.] *Rev. Asoc. Med. Argentina* 1945 Mar 30 v. 59 No. 654 288-73 3 charts [11 refs.]

Thirty-five cases were subjected to treatment. 4 were of septicaemic and 31 of bubonic type. There were five deaths all bubonic and in four of these cases there was the complication of plague meningitis. The dosage of sulphathiazole was high: 10 to 12 gm. per day for adults and 5 to 7 gm. for children administered by the mouth and maintaining a concentration in the blood of over 8 mgm. per 100 cc. for not less than six days. As auxiliary to this treatment patients received vitamin B₁, desoxyvorticosterone and normal glucose saline. It was important to keep the patient well supplied with fluid to drink.

W. F. Harter

CHOLERA

PANJA, G. Treatment of Cholera with Atebrin. *Indian Med. Gaz.* 1945 Mar., v. 80 No. 3 133-4

Dyes such as brilliant green and malachite green have been found to be both bacteriostatic and bactericidal to cholera vibrios, but in practice they are rendered inactive by the alkaline contents of the intestine. This is not the

case with atabrin which was found to be bacteriostatic in dilution of 1-4 000 to cholera vibrios of Inaba and Ogawa strains. It is not bacteriostatic however to paracholera or saprophytic vibrios nor to enteric and dysentery bacilli. Experimental guinea pigs prepared for cholera infection by starvation and administration of sodium bicarbonate opium and atropine were used with appropriate controls. The control animals died while those given atabrin survived, the intragastric testing dose of *V. cholerae* being 15 cc of young broth culture. Twenty human cases of cholera were treated with atabrin in a dose of one tablet [presumably 0.1 gm] every 15 to 30 minutes until four to six tablets had been given on one day. Some patients received two more tablets on the following day. It was found necessary to give these patients hyper-tonic saline on admission which was late in the collapsed stage. Nineteen of the twenty patients survived which is a very satisfactory result. Eight patients treated with quinacrine in whom the results were not so encouraging may be taken as a control series.

W F Harvey

SEN A N & BASU U P Synergistic Effect of Sulphanilyl Benzamide on *V. cholerae* Bacteriophage. *Indian Med Gaz* 1945 Apr v 80 No 4 194-6

In this investigation the bacteriostatic action of sulphanilyl benzamide (a sulphonamide derivative) has been determined and also its influence on the lytic action of cholera bacteriophage. A stock solution of one grammme of the powder in 100 cc. water at pH 8.0 was used to make appropriate dilutions. In the first place it was found that the drug in limiting dilution of 1 in 20 000 exerted no action on the cholera vibrio. The second step was to determine whether this dilution could exert any bacteriostatic action on secondary growth after stock bacteriophage had destroyed a partially susceptible strain of *V. cholerae*. It is this action which is describable as synergistic. Special tests showed that the drug had no destructive action on the lytic action of the phage itself. Results obtained seem to indicate that the drug acts only on the vibrios which are not lysed by the bacteriophage. These same vibrios however on culture did not differ apparently from the original strain in morphology and smoothness nor were they acted on by the drug in the dilution used. Thus it would seem that the lytic action of the phage is synergistically increased in the presence of the drug, and that a combination of the two agencies, sulphonamide and phage might be useful in the treatment of cholera.

W F Harvey

WAR MEDICINE, Chicago 1945 June v 7 No 6 371-6 Cholera War Department Technical Bulletin TB Med 138

BACILLARY DYSENTERY

WALL R. & GARVAN J M. Dysentery in the Northern Territory. *Med J Australia*. 1945 Apr 28 v 1 No. 17 428-9

Bacillary dysentery due to Flexner bacilli is endemic throughout the Northern Territory of Australia. the present report relates to the treatment with sulphaguanidine of 101 acute cases and 13 carriers the dosage being as follows — an initial dose of 7 gm. followed by 3.5 gm. every four hours until there were less than five stools in 24 hours then 3.5 gm. every eight hours until a normal number of stools were passed on each of two successive days the total dose to be not less than 70 gm. In the 101 acute cases the average total dose was 104.7 gm. given in an average period of 8.1 days

Carriers were given 3.5 gm. every four hours for three days, then every eight hours for four days i.e. about 109 gm. in a week.

Five patients had a toxic rash and headache and three had slight fever. In one patient sulphonamide crystals were found in the urine.

It was found by trial that a fairly full and varied diet could be taken from the beginning without ill-effects. It included soups, porridge, sago, rice, blanc mango, junket, steamed puddings (without suet), eggs, liver, brain, fish, minced meats, vegetable *purées*, tinned and stewed fruit, toast, bread, biscuits and small amounts of butter: the fats to be kept low. No fresh milk was available. A fluid intake of 4½ litres in 24 hours was aimed at.

The only complications were transient pain and tenderness near joints and recurrence of diarrhoea (15 cases) about a week after the end of sulphaguanidine treatment.

Stools and rectal swabs (143 of each) were examined bacteriologically at various intervals from 5 to 30 days, after completion of the course of sulphaguanidine: no dysentery bacilli were isolated. In the 101 acute cases sigmoidoscopy showed a normal rectal mucous membrane after, on the average, eight days from the end of the sulphaguanidine course.

Prolonged observation after treatment was not possible as it was necessary to return the patients to duty as soon as possible.

J. F. Corson

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

✓ LIEBERMAN, H. R. Carrier Rate of Intestinal Parasites in the Non-European Staff of a Military Hospital in Natal, with special reference to *E. histolytica*. *South African Med. J.* 1945 July 14 v. 19 No. 13 231-3.

The persons examined were mostly Africans with a few Indians: they were employed in general work in the kitchens, wards, messes and grounds of the hospital. A fresh preparation of faeces in saline and in iodine was examined microscopically: no concentration methods or staining being used.

Among those engaged in handling food in the main kitchen, carriers of cysts of *Entamoeba histolytica* were found, and the same result was obtained in other departments where food was handled. Ova of *Ascaris* and *Trichuris trichiura* were also present in food handlers, and in one case *Ancylostoma*.

Thirty-one of the 105 males showed cysts of *E. histolytica* and 38 showed helminth ova—*Ascaris* (31), *Trichuris trichiura* (34), *Taenia* (2) and *Ancylostoma* (2). No cysts of *E. histolytica* were found in the females.

J. F. Corson

CATAN, T. The Pathogenicity of the *Amoeba histolytica*. *J. Roy. Egyptian Med. Ass.* 1944 Oct v. 27 No. 10 448-57.

A thorough macroscopical examination of the fresh faeces of 400 patients at a Jerusalem hospital was made to determine the incidence of infection with *Entamoeba histolytica*: 122 (30.5 per cent.) were infected. The relationship of infection to the presence of abdominal symptoms was examined in 356 of these patients: 101 had symptoms of acute intestinal inflammation, 75 had mild symptoms of indigestion, and 180 had no abdominal symptoms. *E. histolytica* was found in 27 (26.7 per cent.) of the first group, in 36 (48 per cent.) of the second, and in 40 (22.2 per cent.) of the third group.

The author concludes that in Palestine the rate of infection is about the same in persons with symptoms of acute intestinal inflammation as in persons with

no abdominal symptoms. From long experience in a German hospital in Palestine he has learned that amoebic dysentery is comparatively rare among the Palestinian Arabs the hospital records show that there were only 11 cases of amoebic abscess of the liver among 9 690 in patients from April 1934 to May 1939 These findings have an obvious bearing on the diagnosis and treatment of cases with intestinal symptoms

J F Corson

BELTRÁN E. Influencia del sexo en la incidencia de protozoarios intestinales humanos especialmente *Endamoeba histolytica* [The Influence of Sex in Infection with Human Intestinal Protozoa, especially *E. histolytica*] *Rev Inst Salubridad y Enfermedades Trop* Mexico 1945 Mar v 6 No 1 31-6 [21 refs.] English summary

Results of investigations carried on by the author as well as those from others are presented in relation to any possible sex difference in parasitation for human intestinal protozoa generally and specially by *E. histolytica*

Consideration of the parasitological findings in 16 435 subjects does not seem to show any definite relation between sex and parasitation.

Considering the possible avenues of infection the author's opinion is that the differences found in distinct surveys are due to peculiar living conditions of the groups considered rather than to any more or less susceptibility in one or another sex.

HARGREAVES W H Chronic Amoebic Dysentery A New Approach to Treatment. *Lancet* 1945 July 21 68-72. [14 refs.]

After referring to recent papers by ADAMS [this *Bulletin* 1945 v 42 559] and by LAMB & ROYSTON [*ibid* 561] and to his own contribution to the discussion on Adams's paper [*ibid* 560] where he describes the experience now given in the present paper the author relates the history of specific treatment of amoebiasis concluding that no evidence exists to show that any specific drug is equal to emetine bismuth iodide (E.B.I.)

During the past year the author's standard treatment has been as follows a 12-day course of E.B.I. together with retention enemata of chiniofon [yatren 105 quinoxyl] followed by stovarsol or carbarsone grams 4 *bis die* for 12 days if there were dysenteric symptoms this was preceded by six daily injections of emetine hydrochloride gram 1

The 21-day blunderbuss treatment of the Liverpool School of Tropical Medicine is as follows on the odd-numbered days auremetine [a combination of the periodides of emetine and auramine ($C_{17}H_{21}N_3ClHO$)] 1 gram *t.d.s* bismuth carbonate 1 drachm *t.d.s* on even days—at 8 a.m. a rectal wash-out with 2 per cent sodium bicarbonate at 9 a.m. the foot of the bed being raised a retention enema of 2 per cent quinoxyl [chiniofon] by a catheter (half way through the course the strength becomes 4 per cent) stovarsol tablet grams 4 *t.d.s* bismuth carbonate 1 drachm *t.d.s* The patient stays in bed on the even days and is allowed up on the odd days if well enough. A glucose drink (1 lb of glucose to 1 quart of barley water or lemonade etc.) is given, and a normal diet avoiding indigestible foods.

The author compared the two forms of treatment each on 40 patients of those receiving E.B.I. six were not cured, while of those receiving the Liverpool School course 21 were not cured. He concluded that in spite of its unpleasant action E.B.I. should be given daily

The existence or development of emetine-resistant strains of *E. histolytica* has been accepted by ADAMS LOURIE and others but the researches of DOBELL *et al* [this *Bulletin* 1918 v 12, 5] did not support that view and in the author's opinion there is no reliable evidence that they can be produced.

He then describes his experience of treatment of amoebic dysentery, amplifying his earlier account [*loc cit.*] he treated 268 patients during the past year about one fifth of them having severe symptoms and some being desperately ill. Many patients from Burma had had amoebic dysentery since 1942, and most of the patients had had repeated courses of E.B.I. but it had almost always been given in a badly absorbable form such as pills or tablets. The author points out that in spite of repeated condemnation, E.B.I. is still made and administered in keratin-coated tablets.

These patients responded poorly to the standard treatment and the author as previously reported [*loc cit.*] tried penicillin and succinyl-sulphathiazole sulfasulidine. The former was given in a total dosage of 2 million units intramuscularly (100 000 units as the initial dose followed by 33 000 units 3-hourly) and the latter by mouth in a total dosage of 80 gm. The results were very good apparently by action on secondary infections and not on the amoebae.

In the second week of treatment three daily specimens of faeces were examined and sigmoidoscopy done. If the result was satisfactory the patient was sent away for a month's convalescence and if he kept well he was readmitted to hospital and six daily faecal examinations and a sigmoidoscopy were made. On his discharge he was given follow-up cards for reporting by post.

Notes of 10 illustrative cases are given.

Penicillin was also tried with success in five cases of chronic ulcerative colitis.

J. F. Corson.

VARIL, R. J. Tolerance to Enterovioform Tablets. *Indian Med Gaz.* 1945 Mar 1, 60, No 3 147-8.

The active substance in enterovioform is vioform (iodochlorhydroxy quinoline) which has been used with success in the treatment of amoebiasis in man (this Bulletin 1934 1 31 285). The author records the case of a patient whose symptoms appeared to have been the result of taking enterovioform continuously for a long period.

A man, aged 35 complained of increasing lassitude and fatigue on slight exertion, headache and mental depression, which began two months before in June 1944. On examination he showed great nervous irritability and a fine tremor of the outstretched hands. The first heart sound was less loud than normally. The pulse rate was 116 per minute and the blood pressure was 104/80. No other signs of disease were found.

In the middle of 1943 he was ordered to take six enterovioform tablets daily by mouth for diarrhoea or dysentery and was cured of his symptoms in a fortnight. He chose however to continue taking the tablets without a break until August 1944 and had then taken 2,000 tablets.

He was treated by rest in bed, a light diet, digoxin and coramine tablets, and intravenous injections of glucose and was cured in three weeks. The first heart sound became normal, the pulse rate 70 per minute, and the blood pressure 132/78.

J. F. Corson.

WAR MEDICINE, Chicago 1945 June 7 No 6, 390-96. Amoebiasis. War Department Technical Bulletin TB Med 159.

WAR DEPARTMENT TECHNICAL BULLETIN. Wash. D.C. 1945 Aug 1 8 pp. Water Treatment in Areas where Amoebiasis and Schistosomiasis are Hazards. (TB Med 199.)

FRASER J F & TAYLOR R. *Diarrhoea due to Giardia lamblia* *Brit Med J* 1945 Aug 11 184-5

Among 872 cases of diarrhoeal diseases treated in a British general hospital in India *Giardia intestinalis* was the sole apparent cause in 21 and was present also in four cases of bacillary dysentery and in four of amoebic dysentery. All the 21 patients had diarrhoea and 15 complained of colic which was relieved by evacuation of the bowels. Tenesmus was present in one case only. In nearly all the stools were watery, faecal rather paler than normal and generally appeared greasy in two cases blood and mucus were present. The duration of symptoms before admission to hospital varied from 1 to 35 days but in most cases it was a few days only. Treatment with mepacrine—0.1 gm. t.d.s. for five days—cured all except two and a second course cured these. All the patients were given a generous diet and symptoms disappeared by the third day of treatment.
J F Corson

HEMMING G R. *Giardiasis associated with Recurrent Rectal Haemorrhages* [Memoranda] *Brit Med J* 1945 Aug 11 185

A female child, aged four years was admitted to hospital at Suva, Fiji on March 13 1944 with a history of fever constipation weakness and passage of blood with the stools. Physical examination revealed no abnormality but she continued to pass blood until her discharge to the out patient department on May 6. The blood passed was sometimes clotted sometimes bright red and mucus was often present. The stools were soft and pale and there was often diarrhoea. No parasites were found in the faeces and sigmoidoscopy showed no abnormality. Her blood contained 3 100 000 erythrocytes per cmm. and haemoglobin 80 per cent.

She was readmitted with the same symptoms six days later. Examination of the stools on various dates showed infestation with *Trichuris* and hookworm and on May 27 a heavy infestation with *Giardia intestinalis*. On June 1 her blood showed 2 800 000 erythrocytes and haemoglobin 60 per cent. Treatment was given for the anaemia, and mepacrine 3/4 gram t.d.s. for five days was given for the giardiasis and was repeated after 10 days. No blood appeared in the stools after the first course of mepacrine and the patient was discharged on June 22.
J F Corson

SEGAL, M. *Giardiasis* Report of a Case. *South African Med J* 1945 June 23 v 19 No 12 213

Cysts of *Giardia intestinalis* were present in the faeces of a male child aged 16 months who had been suffering from diarrhoea for a month. On admission to hospital he was much wasted. The stools were bulky loose clay-coloured and foul-smelling—exactly similar to those seen in coeliac disease. The urine was normal. The temperature was 100 F.

A fat free diet was ordered to be given at first cautiously then as the child was ravenously hungry more liberally. Elixir Bevin and sulphaguanidine were also prescribed. Improvement was prompt and rapid and the child left hospital after six days and had remained well when seen again a fortnight later.

When the laboratory report of the presence of cysts of *Giardia intestinalis* was received the sulphaguanidine was replaced by atabrin (as Quinacrine) which was given for five days but as marked improvement had already taken place it is doubtful if this had any effect.
J F Corson

RELAPSING FEVER AND OTHER SPIROCHAETOSSES

ANDREY L. A. [Tick-borne Relapsing Fever in Kazakhstan.] *Ved. Parazit. & Parazitich. Dis.* Moscow 1944 v. 13 No. 3 53-7 [In Russian.]

Although the presence of tick-borne relapsing fever in Kazakhstan [Central Asia] has been suspected for some time there have been no records of its incidence or of the occurrence of the tick vector in this region. The author reports the results of a survey carried out by the local Tropical Institute in 1940 with the object of throwing light on the distribution of this disease in Kazakhstan. It was shown that the distribution of the vector *Ornithodoros papillipes* was restricted to the basin of the river Chirchik in the Bostandyk district, in which a number of villages proved to be foci of relapsing fever. C. A. Hoare

i. HEILMAN F. R. with the technical assistance of Mary KNUTSON & Nellie GREENBURG. Streptomycin in the Treatment of Experimental Relapsing Fever and Leptospirosis Ictero-haemorrhagica (Weil's Disease). *Proc. Staff Meetings Mayo Clinic* 1945 May 30 v. 20 No. 11 166-76. [27 refs.]

ii. — with the technical assistance of Mary KNUTSON & Nellie GREENBURG. Addendum to Streptomycin in the Treatment of Experimental Relapsing Fever and Leptospirosis Ictero-haemorrhagica (Weil's Disease) *Ibid* June 18 v. 20 No. 12, 183.

i. Experiments were made to test the action of streptomycin on relapsing fever (*Spirochaeta nova*) in mice and on leptospirosis (*Leptospira icterohaemorrhagiae*) in hamsters.

Relapsing fever—A total of 100 Swiss mice were infected by intraperitoneal injection of various amounts of blood of a rat or mouse infected with *S. nova*. On the following day when all the mice showed infection in the blood, 50 were given subcutaneous injections of streptomycin—each mouse received 1 000 units a day for four days in divided doses in normal saline—150 units at 9 a.m., noon, 3 and 5 p.m. and 400 units at 9 p.m. In two experiments the 9 p.m. dose was given in beerwax and sesame oil. Thick smears of tail blood, stained with Giemsa's stain, were examined on the 1st, 2nd, 3rd, 4th, 7th, 8th, 9th and 11th days after inoculation.

Spirochaetes were not found in the blood of one untreated and 15 treated mice 24 hours after the first injection or in 22 untreated and 35 treated mice after 48 hours. Numerous spirochaetes were present in the blood of 10 treated mice 24 hours after the first injection. This result was not so good as that obtained with penicillin [this *Bulletin* 1944 v. 41 758].

During the 11 days of observation there were five relapses in the 46 surviving treated mice and 34 relapses in the 40 surviving untreated mice, but the observation period was short as relapses in the treated mice appeared on the 11th day and in the untreated mice on the 7th day.

Four of the 50 treated mice and 10 of the untreated mice died—the latter figure indicates that the virulence of the infection was lower than that in a similar experiment with penicillin where 21 out of 23 untreated mice died.

Experimental Weil's disease—Fifty hamsters (*Cricetus auratus*) were infected by intraperitoneal injection of the blood of a guinea-pig in the acute stage of the disease. Twenty-five were given subcutaneous injections of 1 000 units of streptomycin in saline daily beginning 17 hours after inoculation and continuing for 10 days—each received 200 units at 8 a.m., noon, and 4 p.m. and 400 units at 9 p.m. All the treated animals remained well and all the untreated animals died. Inoculation of emulsions of the organs of the treated animals into guinea-pigs and hamsters failed to infect them.

Another experiment was made to compare streptomycin with penicillin a preliminary test having shown that the injection of penicillin produced no ill effects in hamsters. Three groups of 12 hamsters were used and there were 12 controls six of each group were injected with streptomycin and six with penicillin in divided doses at 9 a.m. noon 3.5 and 9 p.m. daily for 10 days. The doses were 250 units for each of the first group 500 for the second group and 800 for the third.

In Group 1 all the hamsters died in Group 2 none of the six injected with penicillin died and four of those injected with streptomycin died and in Group 3 none died. All the control animals died.

The author concludes that streptomycin had a considerable protective action in both infections but that penicillin was more effective. He suggests that streptomycin may be a useful adjunct to penicillin in the treatment of spirochaetal infections in man. [See also this *Bulletin* 1944 v 41 293 759 & 942 1945 v 42 210 & 387.]

ii The author adds the comment that since the unit value for penicillin and that for streptomycin were established on a different basis it may be misleading to compare their action by the numbers of units needed to cure an experimental infection.

J F Corson

YAWS

KATZENSTEIN L. A Case of Yaws In a White American Soldier. *Amer J Syph* 1945 May v 29 No 3 340-44 4 figs

A white American soldier was admitted to hospital on March 15 1944 suffering from yaws of three months duration which was acquired in New Guinea or neighbouring islands where he had been in military service for nine months. The primary yaw appeared in the first week of December 1943 as a pimple on the dorsum of his right foot secondary lesions were first noticed in the middle of February 1944 in his right axilla and on admission to hospital he had brownish yellow crusted papules distributed over his whole body but chiefly on his legs.

The blood test for syphilis was positive and spirochaetes resembling *Sp. pallida* were present in the papules the cerebrospinal fluid contained 0.035 per cent of protein one cell [per cmm ?] the colloid mastic test gave 11111 00000 and the Eagle complement fixation test was negative.

The histological characters of an excised yaw are described there were tiny abscesses in the epidermis and a plasma cell infiltration of the dermis but no perivascular lymphocytic infiltration such as is seen in syphilis. Intratesticular inoculation of rabbits with material from a papule failed to infect them.

The patient was treated with mapharsen six doses of 0.06 gm. during three weeks and two doses of 0.2 gm. of bismuth subsalicylate. Healing of all lesions was complete in three weeks.

J F Corson

LEPROSY

ALEXANDER JACKSON Eleanor. Non-Acid Fast Forms of the *Mycobacterium* of Human Leprosy. *Science*. 1945 June 1 563-4

The author reports the results of staining material containing the mycobacterium of leprosy with her triple stain (see *Bulletin of Hygiene* 1944 v 19 806 for its composition) which reveals non acid fast forms of the tubercle

bacillus. A number of unfixed films of nasal material from a case of leprosy so stained revealed not only red-stained acid fast bacilli, but also blue-stained non acid fast rods in even greater numbers. Nests of rods may show mixtures of both types but many nests consisted of blue-stained rods only. Fixed unstained smears from leprosy skin biopsies from 32 different cases were next treated with the triple stain and examined with the following results: 27 (84.4 per cent.) showed zoogloal and granules or spore-like forms; 16 (50 per cent.) showed zoogloal forms only; 13 smears (40.6 per cent.) showed some acid fast forms; 11 smears (34.4 per cent.) showed acid-fast or non-acid fast rod forms. There were no differences in the findings in patients with different dates of admission but the oldest admitted 24 years ago showed only non-acid-fast zoogloal forms. In six neural and tuberculous cases zoogloal forms and rods were absent. These results strongly suggest that the leprosy bacillus like the tubercle bacillus has a zoogloal form or phase. Further observations with the use of the triple stain are indicated.

L. Rogers

TROUT C. L. The Cultivation of the Leprosy Bacillus. *J Trop Med & Hyg* 1945 Feb. Mar v 48 No 1 8-9

The author has succeeded in obtaining a pure culture of an acid-fast organism by inoculating a Difco agar medium (containing glycerin) with an emulsion obtained by injecting saline into a leprosy and withdrawing it into the syringe. The emulsion contained many acid-fast organisms. During incubation [presumably at 37°C] carbon dioxide was passed over the medium. The emulsion was kept in the syringe in the incubator for six weeks before inoculation of the medium; by that time filaments had appeared in it.

The author has also grown acid fast organisms isolated in previous experiments, in a Difco broth medium through which ammonia gas or carbon dioxide was bubbled.

Charles Willocks

DIARMEDIA & MUMBERJI. Attempts to transmit Human Leprosy to Splenectomized Monkeys. *Indian J Med Res* 1944 Oct v 32, No 2 197-200

After a brief review of previous claims to have infected splenectomized monkeys with human leprosy material, the authors record their own experiments. In the first series six *Macaca rhesus* (*Macaca mulatta*) had their spleens removed under chloroform and after recovery each animal was inoculated intraperitoneally with an emulsion of clippings from the ear lobes of advanced lepromatous cases and the inoculation was repeated after two months. External examinations were made with negative results, and leprosy tests were carried out 16 months later without producing any reaction at the site of inoculation. Post-mortem examination revealed no gross pathological lesions suggestive of leprosy infection nor were there any acid fast bacilli in slightly enlarged glands in one animal, or in a suspicious nodule found in the omentum of another. Claims (COCHRANE *et al* *Internat J Leprosy* 1937 v 7 377) to have obtained positive results through such inoculations were therefore not confirmed.

L. Rogers

BECHELLI, L. M., KEIL, H & ROTBERG A. Resultados da lepromino-reação em países não endêmicos de lepra (Nota Preliminar) [The Lepromin Reaction in Countries where Leprosy is not Endemic. *Rev Brasileira Leprologia* S Paulo 1945 Mar v 13 No 1 21-4]

BURGHER, DE LANGEN and others have regarded positive lepromin reactors among healthy individuals in countries where leprosy is endemic, as suffering from a subinfection owing to contact with patients.

The authors have tested the reaction among those who have never run the risk of any such contact and have compared the results with the Mantoux tuberculin test among those attending the Skin and Cancer Clinic of the New York Post-graduate Medical School. The results are given in tables from which the conclusions may be thus summarized. The delayed lepromin reaction does not necessarily imply a latent infection. Its specificity is nevertheless upheld by regarding the positive reaction as allergy to the lepromin developing in the three to four weeks elapsing between the injection and the recording of results. WADE had previously observed positive reactions in non-contacts and explained this by saying that such persons react allergically on coming into contact with Hansen's bacillus.

The early reaction occurring in 12 hours or less may also be observed in non-contacts and the above explanation obviously cannot be applied to these. It has been suggested by FERNANDEZ and others that tuberculosis may be accountable for such. The authors' findings in their cases here recorded (38 only so far) support this interpretation for in all but one of those giving this early lepromin reaction the Mantoux reaction was also positive. [This short paper is only preliminary further results will be awaited with interest.]

H Harold Scott

AMENDOLA F. A glândula lacrimal na lepra ocular. [The Lacrymal Gland in Ocular Leprosy] *Rev Brasileira Leprologia* S Paulo 1945 Mar v 13 No 1 3-11 1 pl

The treatment of eye affections in leprosy is far from satisfactory and in spite of all that is done often fails to prevent total blindness ensuing. On an analogy with other inflammatory conditions determination of the focus and its removal are of primary importance. The lacrymal glands though they may be few nevertheless by their continuous secretion if infected are a constant source of reinfection and consequently of great moment in the evolution of leprotic lesions of the eye.

The author quotes the case of a patient who had undergone three operations for ocular lepromata in six months each in turn followed by a relapse. It was decided to extirpate the lacrymal gland and the result was a resolution of the congestion and the ocular lesions.

Appended to the article are brief notes of 20 cases nearly all the patients had had treatment of all kinds without lasting benefit and had then submitted to removal of the lacrymal gland. In a few days (three-four) the pain and photophobia disappeared and the patients expressed themselves as feeling better and the general outlook in every sense of the term rapidly improved. The author speaks emphatically in favour of this operation for the ocular lesions of leprosy stating that in the majority of cases histological examination shows that the gland is infected and even in cases in which the pathological anatomy is negative extirpation is not contra indicated because clinically benefit nevertheless follows.

H Harold Scott

DHARMENDRA & CHATTERJI S. N. Trigeminal Neuritis simulating Leprosy. *Leprosy in India* 1945 Apr v 17 No 2 40-43 2 figs

AMENDOLA F. A traqueotomia na lepra. [Tracheotomy in Leprosy] *Rev Brasileira Leprologia* S Paulo 1945 Mar v 13 No 1 27-30

The circumstances in which tracheotomy is undertaken in lepers differ from those in other non leprosy patients, for in the latter the operation is a matter of immediate urgency on account of acute obstruction as in laryngeal diphtheria an impacted foreign body acute oedema and such like whereas in

lepers, in nearly all cases, the operation is undertaken without haste in cases of gradually increasing obstruction, and the earlier stages have been treated by cantery for example or removal of a leproma. Again the site is often analgesic so there is less need for general anaesthesia but on the other hand, if general anaesthesia is needed there is no little risk on account of cardiac or pulmonary disease. Hence there is often need for preliminary administration of cardiac tonics. The low operation is to be preferred. A second operation some time later may be required, although the tube is in good position. This is due to the formation of a thick mucro-membranous exudate below the cannula which is difficult to remove. The operation is then one of urgency and death may occur before relief is obtained.

The author's remarks are based on 29 cases. 11 patients died [but a table gives 10 only] two during the operation one from syncope the other owing to the advanced stage of his disease and the operation could not be completed. Of the others one died a month later one six months later three lived for a year two for 2½ years and one for 3 years. All these died from cachexia due to the leprosy or from intercurrent maladies.

H. Harold Scott

ALLER ATUCHA J. F. Sulfatiazol en las manifestaciones leprosas. Mácula—Infiltración—Lepromas—Pénfigo—Úlceras—Conjuntivitis—Saturación sanguínea [Sulphathiazole in Leprotic Lesions.] *Rev. Asoc. Med. Argentina* 1945 May 16 v. 59 No. 557 497-505 12 figs.

The work which this article records was carried out in 1942 and was reported at the Second Medical Congress in the Argentine. The results which the author mentions are in some cases little short of miraculous as for example cicatrization of a perforating ulcer of the foot in five days but nothing is said of their permanency only the immediate results are told. The drug was used as a 15 per cent. jelly or as a 10 per cent. oily suspension, or a 15 per cent. watery emulsion (*crema acuosa*). For extensive and generalized lesions a 5 per cent. sodium salt was injected intravenously.

Various forms and stages of the disease were thus treated and a short note of a few lines is given on each case. First, the macular three in number the places were scraped once a week and then the watery preparation was rubbed in three or four times daily for 1-3 months. Two improved the third made no progress. Five cases of leprosy infiltration all showed great improvement in 2-4 months by three or four rubbings daily with the same preparation. Two patients with lepromas were treated the leproma in each case was incised, the contents evacuated and the jelly preparation then applied. Cicatrization was complete in 10 days in the one in 15 in the other. Patients with ulcers of various sizes and depth were treated with the jelly for periods up to 3½ months. In one with multiple ulcers of the right thigh and knee all the ulcers were completely cicatrized in 11 days. Those with eye lesions the author divides into (i) Hyperacute in which the sequence of events is rapid, with diffuse keratitis iris exudation into the anterior chamber haemorrhage and intense pain leading soon to blindness. Two cases of this type are mentioned the oily suspension was used and in 16 and 14 days respectively sight was perfect and the treatment was stopped. (ii) Acute in which the symptoms were similar but less severe one case only of this is reported. In two months the subjective symptoms disappeared and vision improved. (iii) Subacute with small infiltrations and nodules affecting also the lids, with conjunctivitis and indo-cyclitis one case which improved in ten weeks the patient stating that whenever treatment was suspended the symptoms recurred. (iv) Chronic with plastic changes 19 cases mentioned, of which 13 improved while 6 remained unaffected.

One patient a woman of 51 years had generalized lesions on face neck trunk and limbs maculae and infiltrations. She was given injections of 20 cc. intravenously every six hours for four days then every eight hours for the same period then every 12 hours for another four days. She was also given chaulmoogra 5 cc. and propidon every four days altogether she had 36 gm. of sulphathiazole (with a blood-content of 4 mm per cent [so stated]) 30 cc. of chaulmoogra and three ampoules of propidon. She tolerated the drugs well and 4½ months after the first course she underwent a second and four months later a third. The maculae presented a modification in colour and shape very few fresh lesions appeared and during the whole period one year the leprosy reactions were fewer and less intense.

H Harold Scott

DHARMENDRA & MUKHERJI N The Effect of Sulphapyridine on Experimental Rat Leprosy *Indian J Med Res* 1944 Oct v 32 No 2 201-3

Variable results have been reported by different experimenters as to the effect of sulphonamides on rat leprosy bacilli. The authors report on a trial of sulphapyridine (M & B 693) ground up and suspended in normal saline and injected through an oesophageal cannula into the stomachs of rats. The dose was 10 mgm daily gradually raised to 40 mgm in white rats weighing 80 gm. The administration was commenced two or three days before inoculating the animals with the infective dose of bacilli and was continued for several days and after two weeks interval 10 to 20 mgm were given daily for another 2½ months. In the first series 18 were so treated and 20 used as controls but no differences in the nature or extent of the lesions were found. A second series with slightly different doses also yielded negative results. The drug therefore does not appear to have any inhibitory effect *in vivo* on *Mycobacterium leprae muris* although *in vitro* it has been shown to have a bactericidal effect in a dilution of 1 in 1,000.

L Rogers

FIELDING J W Rat Leprosy Observations and Transmission. *Med J Australia* 1945 May 12 v 1 No 19 473-86 18 figs. (12 on 1 pl) [Numerous refs.]

This is a detailed, and well illustrated, account of comprehensive investigations the value of which is enhanced by brief summaries of earlier work on each point dealt with and a full list of references. It brings out some important points and should be read in full by research workers.

After reference to the geographical distribution of rat leprosy the distribution of the causative organism in the body is dealt with. A number of heavy infections of the sternum are recorded. Infection of glands is variable and most frequent in connexion with invasions of the skin. The author confirms the observation by KRAKOWER and GONZALEZ (*Science* 1937 Dec. 31 617) of lepra cells in the pancreas. He has also found graded infection of the stomach pylorus and duodenum which is very much heavier in experimentally infected rats than in those naturally infected. Moreover the organisms in the faeces are so numerous that they can no longer be regarded merely as elimination products for all infected rats kept for a long period show heavy faecal infections. Microscopical examinations of the whole of the alimentary tract from the tongue to the anus were therefore made they revealed heavy infections of the stomach, with destruction of the mucosa at the cardiac end and a progressively decreasing infection through the pylorus to the duodenum. The rest of the tract was either unaffected or contained only scattered loose organisms. Contrary to the opinion of LOWE (this *Bulletin* 1938 v 35 302) the author found that repeated inoculation of intact skin with emulsions of the

rat leprosy bacilli resulted in extensive bacillary invasion of the skin associated with clinical lesions with intracellular organisms long before extensive internal lesions could occur. As faecal organisms had been found capable of infecting rats through the skin those portions of the surface of the body in contact with the ground were examined, and in most experiments definite invasion of the skin by the organisms was found. The distribution of the organisms is therefore much more general than has hitherto been realized. For to the list put forward by various authorities the following localities should be added: stomach, pylorus, duodenum, pericardium, bulbo-urethral and preputial glands (he only examined male rats) and sternum. A link has also been provided between soil contamination and dissemination of the disease as suggested by WALKER and SWENLEY this *Bulletin* 1929 v. 26 1032. Evidence is also recorded to show that the urine commonly contains over a million rat-leprosy bacilli per cc. and the faeces far larger numbers.

Microscopical work indicates that the lepra cells in superficial lesions arise from polymorphonuclear leucocytes the nuclei of which become gradually destroyed with the multiplication of the bacilli in the cells. Of greater interest are the author's observations on the virulence and viability of the organism. The resisting power of the rat leprosy bacillus is shown by the fact that those obtained from the faeces of infected animals are equally capable of producing infection through the skin after contact with antiformin for 24 to 48 hours. Moreover fresh faecal organisms appear to be much more constant in virulence than organisms from urine or those of primary ulcers. His results indicate that the bacilli of granukemata and long-standing ulcers have a low standard of virulence while the virulence of organisms from primary ulcers, urine and faeces is on a higher plane. For the production of superficial lesions two things are necessary: first breaking down of local and general resistance by repeated infection or subcutaneous inoculation of the organisms of various types; and second, the use of organisms of high virulence: the continued inoculation of which can produce both internal and external clinical lesions. Doubtless natural infection in wild animals is the result of repeated contact with soil infected by organisms voided in the excreta of rats. Rat lice may also infect by their bites and emulsions of such lice produce infection when inoculated into rats.

Resistance and immunity are next dealt with. When organisms of low virulence are used to infect by inoculation at long intervals the early lesions thus produced completely disappear in time probably as the result of the production of immunity in the animals. In experimental rat leprosy, vitamin B₂ deficiency had no demonstrable influence on infection. In laboratory animals bacilli usually appeared in the urine about 260 days after primary inoculation. Faecal organisms given by the mouth in water did not infect. Hookworm larvae can take up the bacilli present in faecal cultures and infections can be produced by the agency of these larvae which rapidly penetrate the skin of an animal.

L. Rogers

- DE SOTTA ARAUJO H. C. Infecção experimental de carrapatos (*Amblyomma cajennense*) em ratos com lepra Stefanaky [Experimental Infection of *A. cajennense* with the Bacilli of Rat Leprosy] *Mem Inst. Oswaldo Cruz.* 1943 v. 38 No. 2, 183-6 2 figs. English summary (5 lines).

- LINHARES H. Verificação de lepra murina na cidade do Rio de Janeiro. Sua distribuição geográfica e considerações endemológicas. Confirmation of the Presence of Rat Leprosy in Rio de Janeiro. *Mem Inst. Oswaldo Cruz.* 1942, v. 37 No. 3, 353-73 39 refs. English summary.

HELMINTHIASIS

CORT W W The Germ Cell Cycle in the Digeneic Trematodes. *Quart Rev Biol* 1944 Dec. v 19 No 4 275-84 [23 refs.]

This paper is a valuable critical review of our knowledge of this subject. Explaining that earlier workers regarded the multiplication of individuals which occurs in the germinal sacs (mother and daughter sporocysts) of trematodes as asexual internal budding (metagenesis) Cort refers to GROBBEN'S suggestion that it is heterogony effected by truly parthenogenetic eggs in the germinal sacs and to other workers who have described testes and ovaries in the mother sporocysts of some trematodes (*Bucephalida*). Cort accepts the view originated by LEUCKART that the reproductive cells of the sporocysts and rediae (germinal cells or cells of the germinal line) can be traced directly back to the fertilized ovum of the adult trematode and that they never become true germ cells and are never localized in testes and ovaries. Most recent work (which is discussed in some detail by the author) suggests that all of them arise from one fertilized ovum of the adult trematode and remain separate until they finally form the ovaries and testes of the new adults derived from the cercariae. In other words the fertilized ovum of the adult trematode (zygote) produces sporocysts and rediae by a process of polyembryony which continues throughout the cycle in the molluscan intermediate host. The only true germ cells are the cells of the ovaries and testes of the adult trematodes. These undergo gametogenesis to produce sperms and eggs which have the reduced number of chromosomes. This reduced number is present only in the sperms and ova of the adult never in the cells which produce the sporocysts and rediae. This view requires in Cort's opinion much more investigation carried out on a wider range of trematode species but it is a valuable working hypothesis and is the only one which seems to fit the facts.

The methods by which sporocysts and rediae are produced are discussed. The evidence available suggests that the multiplication of the original zygote produces cells of the germinal line (germinal cells) which reproduce by polyembryony to produce large numbers of cells of the germinal line which remain separate and lie in the body-cavities of the germinal sacs (mother and daughter sporocysts). In the two species most studied (*Paragonimus kellicotti* and *Parochus acanthus*) reproduction seems to be only by direct division of the cells of the germinal line (primary polyembryony) the secondary germinal sacs are rediae and reproduction is more limited than it is in groups like strigeids, schistosomes and plagiorchids, in which the secondary germinal sacs are daughter sporocysts. In these latter groups primary polyembryony is supplemented by secondary polyembryony with the production of peculiar germ masses composed of both unicellular and multicellular components. From these the largest multicellular components break away and develop into daughter sporocysts or cercariae as the case may be. In some species this secondary polyembryony may continue for long periods producing large numbers of individuals. In the Strigeidae secondary polyembryony of germ masses has become the chief method of reproduction in both the primary and the secondary germinal sacs. In schistosomes primary polyembryony of germinal cells in both the mother and the daughter sporocysts plays a much larger part in the multiplication of individuals than in Strigeidae but secondary polyembryony does occur although the germ masses are simpler and more transitory. In plagiorchids there is yet another difference. The primary germinal sacs (mother sporocysts) are complex and produce larger numbers of daughter sporocysts than those formed by any other group yet studied. This is apparently entirely effected by direct division of the cells of the germinal line (i.e. by

primary polyembryony) no germ masses have been found. But in the secondary germinal sacs (daughter sporocysts) primary polyembryony seems to be very limited. Each daughter sporocyst produces very early a single large germ mass and this persists throughout and gives rise to very large numbers of cercariae. Secondary polyembryony is thus responsible for the very large numbers of cercariae produced by this group. Further study may reveal yet other relations between primary and secondary polyembryony or even different mechanisms altogether. Existing evidence suggests that primary polyembryony is the primary method of multiplication and that secondary polyembryony is a secondary adaptation which make possible an extraordinary multiplication of individuals. *G. Lepage*

GILLESPIE H. H. Schistosomiasis (Bilharziasis) and Egyptian Splenomegaly
Amer. J. Clin. Path. 1945 Jan., v 15 No. 1 10-16 14 figs. on 4 pls.

This is a short and clear account of schistosomiasis which was read at a meeting of the American Society of Clinical Pathologists at Chicago on June 10 1944. It is illustrated with 12 photographs nine of which are photomicrographs. The text appears to contain nothing new. *J. F. Corson*

WAR MEDICINE Chicago 1945 June 7 No 6 397-405 1 fig. Schistosomiasis
Japanita. War Department Technical Bulletin TB Med 167

BAYLIS H. A. On the Probable Identity of a Cercaria of the Genus *Diphylobothrium* occurring in Wales and Elze. *Ann. Trop. Med. & Parasit.* 1945 Mar. VI v 39 No 1 41-5 13 refs.

In this paper Baylis describes more fully the adults of the species of *Diphylobothrium* reared experimentally in rats and dogs by DUGUID and SHEPPARD [this Bulletin 1944 v 41 857 from plerocercoids which caused the death from general peritonitis of trout in a South Wales reservoir and those obtained by HICKEY and HARRIS (this Bulletin 1944 v 41 858) from the intestines of gulls and cormorants. Hickey and Harris also found plerocercoids in trout in reservoirs near Dublin. LANSFORTH (this Bulletin 1945 v 42 397) reared the adults from South Wales plerocercoids received from Duguid and Sheppard and also from Dublin plerocercoids received from Hickey and Harris. Both were reared in dogs. Baylis (this Bulletin 1945 v 42, 302, 397) has already expressed the opinion that the adult *Diphylobothriidae* obtained from the Dublin gulls belonged to one species and those obtained from the Dublin cormorants to another and that all the adults reared experimentally by the workers mentioned above strongly resembled the species obtained from the Dublin gulls. He considers that all these adults (except those from cormorants) probably belong to the species *D. dendriticum* (Nitsch, 1824) which is normally a parasite of gulls.

In the paper here reviewed Baylis gives the evidence in favour of this conclusion. It is a valuable clarification of our knowledge of the *Diphylobothriidae* and makes clear the differences between the above species and *D. latum* of man. For a better understanding says Baylis of the specific and other characters of the species of *Diphylobothrium* we need a comparative study of considerable numbers of specimens from naturally infected hosts, and this study might lead to the conclusion that the adult *Diphylobothriids* of birds belong to two species only namely *D. dendriticum* (Nitsch, 1824) and *D. ditremum* (Creplin, 1825). The species obtained by Hickey and Harris from cormorants was very probably *D. ditremum* and, if this is true the cormorant is a new host for this species (see also GIBSON (this Bulletin 1945 v 42, 396) and HARRIS and HICKEY *Nature* 1945 Oct. 13 447).

G. Lepage

DIXON H B F & HARGREAVES W H *Cysticercosis (Taenia solium)* A Further Ten Years Clinical Study, covering 284 Cases. *Quart J of Med* (n.s.) 1944 Oct v 13 No 52 107-21 6 pl figs. [26 refs.]

This excellent paper is so full of interesting and informative matter that it cannot be compressed satisfactorily. Of the 284 cases which are studied here all but four occurred in soldiers or in military families but this figure although impressive is not complete for the period under review nor is such a claim made. Twenty-six per cent of the patients gave a history of tapeworm infestation so that auto-infection appears to be common although the proportion in which the identity of the parasite was established is not stated. The authors point out rightly that tapeworm infestation may be overlooked by the host but mistakes take place in the opposite direction also especially if the patient's own statement has to be relied on, *faute de mieux*. In the reviewer's experience one man when asked to make a rough sketch of the tapeworm segments which he confidently asserted he had passed produced recognizable drawings of several *Ascaris* his honest misstatement resulting from suggestion on the part of some former questioner.

Calcified cysts were detected in the brain in 11 per cent in other words in 89 per cent of proved cases radiographic examination of the skull was negative. Yet it is still common to find that in suspected cases cysticercosis has been excluded on the evidence of a single negative radiograph limited to the brain! In showing up calcification 'high penetration' was found more effective than the slight under-exposure advocated by Morrison. This statement may puzzle a reader not already familiar with Morrison's technique for penetration and exposure are not comparable terms. What he advocated was ordinary exposure conditions for bone detail with a very slight under-exposure. In the experiments which led to the adoption of this standard the reviewer cannot recall any instance in which calcification appreciable to the eye in a parasite removed from the body failed to show in radiographs taken of it *in situ* using the procedure finally chosen as indicated above. If on further trial the authors technique proves consistently superior to that advised by Morrison strictly followed this is a notable advance. The fact remains however that only in a minority of cases do the degenerative changes in intracerebral parasites go on to calcification.

The reviewer is charged with having painted too gloomy a picture of this disease. He agrees as regards his original estimate which was coloured by several tragic happenings about that time. This view however was qualified in a later publication where several more favourable types of the disease are recognized. (This article is included in the authors list of references.) Even so he takes a less assured view than is adopted in their assessment where 36 per cent of the cases are classed as showing improvement and 15 per cent as now recovered. In arriving at this estimate no doubt the authors have striven to guard against the known fallacies which have to be borne in mind in dealing with this uncertain and treacherous disease. It might be well to mention some of these disturbing factors for they are not as widely known as they should be. In the seemingly milder type of case the investigator may have to rely mainly or even entirely on the patient's own statements. Those who hope to obtain or fear to lose some job often understate the degree of disability present. Others try to hide it altogether sometimes with surprising success their fits may be nocturnal or infrequent and those who can recognize from some sensation that they are working up for a fit, may manage to disappear for a few hours on some pretext. One man in this last category served as a municipal bus conductor for a long period, and escaped detection. Another man originally invalided from the Army for major epilepsy was

demonstrated to a group of neurologists as an extensive infestation which had never produced any symptoms which shows that the very elect may be deceived. Others quite honestly report themselves as getting on fine or better than I was until some exacerbation changes the picture. Two men in this optimistic group remained under the reviewer's continued observation for about three years each. One in spite of his persistent claim to steady progress (supported by a decrease in his major seizures to about two a year and by full-time employment) developed a sudden left-sided hemiplegia. The other at his final examination as usual reported favourably on his condition, though he mentioned headache for the last day or two. He died three weeks later in a state of wild mania. Again, mental deterioration may be so gradual in onset as to pass undetected even at a medical re-examination and the subject's inaccuracies and omissions may not be realized unless the notetaker knows the correct answers in advance. Moreover the general run of cysticercosis patients are not brain workers nor are their hobbies often of an intellectual type and so a degree of mental retrogression that would be obvious to friends and colleagues in other walks of life may pass unobserved.

Recovery in brain cysticercosis will result if all the intracerebral parasites have died off and degenerated, without causing material and irreparable damage and if organized inflammatory exudates do not undergo some later and hurtful change. At what point the morbid processes in cysticercosis have finally come to an end, unfortunately cannot be determined. The reviewer has seen a cysticercus which had remained alive in the brain for at least 15 years thus with its most dangerous period still before it and even a single parasite suitably situated may cause death or disablement. In his experience relapse has followed symptom free intervals which had lasted for 10, 13 and 20 years. He believes that when a long remission occurs one can but wait and hope for the best while cautiously remembering the scriptural injunction: Judge none blessed before his death.

The foregoing comments and excursions are not meant to detract from this valuable paper and are mainly an elaboration of a few points in the text, introduced in the hope of clearing up some common misunderstandings regarding this difficult subject. The original paper deserves wide circulation and special attention is called to the striking case histories which are given with admirable clarity and effect.

W. P. MacArthur

ARAYA, R. & ASEÑO, A. Ventriculographie Diagnosis of Cysticercosis of the Posterior Fossa. *J. Neurosurgery*, 1945 May v 2, No 3 181-90 11 figs. [24 refs.]

During a period of about three years, 202 cases of "intracranial tumour" were investigated at the Central Institution for Neurosurgery in Santiago, Chile. Twenty five of these proved to be brain cysticercosis. Only in five were the parasites supratentorial in position. The remaining 20 form the basis of this study. In 13 the predominant localization was in the posterior fossa and in 7 the brain invasion was in the fourth ventricle. The diagnosis was confirmed in all cases, either surgically or by autopsy. Four of the fourth-ventricle cases came to autopsy and in these no parasites could be discovered elsewhere in the body, an instructive demonstration of the mischief that one single cysticercus may bring about. In the remaining three the solitary cysticercus was removed from the fourth ventricle and two of the patients were reported "in good condition" six and eight months respectively after operation.

All the 20 cases were studied by ventriculograms obtained by injection of air with the following conclusions —

The X ray findings that point to cysticercosis of the posterior fossa are (1) hydrocephalus (2) absence of displacement of the ventricular system especially of the aqueduct and (3) partial obliteration of the aqueduct and fourth ventricle with presence of air in both and in the cisterna magna. These same features can be observed in cases of single cysticercosis of the fourth ventricle. In the latter the contours of the cysticercus may be outlined.

The reader who is familiar with cysticercosis will notice some curious points in this paper among them the following.—In the great majority of the patients (20 of the original 25) the parasites were infratentorial in situation, the symptoms were exclusively those associated with cerebral tumour—headache, vomiting, eye changes and so forth—with absence of the common cysticercal epilepsy. All the parasites removed by operation or at autopsy were racemose and non-encysted a result of their localization. These are more or less divergences from the usual experience in brain cysticercosis. It looks therefore as if the commoner types which would bring the above more into their proper proportions may not be coming to light. On the other hand, the authors may have made some selection of the type of case required for their particular line of research but this is not indicated in the paper. Perhaps the explanation is that only patients supposed to be suffering from a cerebral tumour were sent to the institute for investigation. W P Mac Arthur

NIÑO F. L. Contribución al tratamiento quimioterápico de la teniasis por *Taenia saginata*. [Contribution to the Chemotherapeutic Treatment of Taeniasis due to *Taenia saginata*.] *Boletín del Instituto de Clínica Quirúrgica* Buenos Aires 1944 Nov.-Dec. v 20 No 168 813-30 [17 refs]

After discussing the unsatisfactory action, toxicity to the human host and other disadvantages of known remedies for infestations with *T. saginata* (male fern, kousoo, kamala, hexylresorcinol, carbon tetrachloride etc.) the author gives the results of his treatment with acranil (Bayer) in 50 subjects. He concludes that acranil is an ideal anthelmintic for these infestations. It is also effective against *Giardia intestinalis*. The author has previously published the results of his earlier treatment of 24 subjects with acranil in *La Prensa Médica Argentina* (1942 v 29 1242) and *Boletín del Instituto de Clínica Quirúrgica* (1942 v 18 279).

Acranil (Bayer) originally called Sostol, is an acridine compound of the atobrin [mepacrine] type with a yellow colour and bitter taste. It is soluble in water and in citric and tartaric acids, very soluble in 1 to 3 per cent HCl, feebly soluble in alcohol and insoluble in very dilute or concentrated NaOH or sodium carbonate. Its toxicity is low. It is marketed in the form of sweetened dragees each containing 0.1 gm., which are easy for even children of three years old to swallow. The adult dose is 0.6 gm. for a single administration but it is better to divide it into two doses. The author gave his subjects 6 to 8 dragees and often gave up to 0.8 gm. without inconvenience to them. These doses can be repeated if necessary after 15-30 days.

The preparation of the patient is very important for the treatment of taeniasis. Two hours after a normal breakfast the subject has a vegetable or mineral laxative. Lunch is bland and light and only liquid diet is allowed after midday. Before sleep a soap and water enema is given and that night half the dose of acranil is administered. On the second day the subject is kept fasting in bed and has the second half of the dose. At 3 p.m. on that day he has 40 gm. of sodium or magnesium sulphate or a castor oil or other purge. After this has acted, the diet is gradually returned to normal. All the faeces are collected and searched for the tapeworm head. Of the 50 subjects thus treated only seven showed symptoms of intolerance of the drug, namely nausea (in five

subjects) vomiting (in two) abdominal pain (in one) diarrhoea (in one) and yellow colouration of the skin (in three). This rarity of toxic symptoms is contrasted with the effects of carbon tetrachloride and other taeniacides in use.

Of the 50 subjects 34 were cured by a single treatment 3 were cured after 2 doses and 1 after 3 doses 3 were not cured 6 were still under observation at the time of writing and the effects upon 3 could not be followed. Thus out of 41 subjects 38 (92·6 per cent.) were cured. The author compares this high percentage of cures with the 97 per cent. of cures claimed by CARMAN [this *Bulletin* 1930 v 27 954] after giving doses up to 4 cc. of carbon tetrachloride and the results of GAMMARA and TALICE (*Octava Reunión de la Soc. Argentina de Patología Regional del Norte* 1934 550) which confirm "the author says Carman's results. He also refers to the use of carbon tetrachloride by DAUBNEY and CARMAN [this *Bulletin* 1928 v 25 932] and by MAPLESTONE and MUKERJI [this *Bulletin* 1932 v 29 414. See also the 80 per cent. of cures obtained with carbon tetrachloride by the same authors, this *Bulletin* 1943 v 40 925] and to the work of GAMMARA (*Arch. Uruguayos de Med. Cirugía y Especialidades* 1934 v 4 583).

The test of cure was either the finding of the head which was found in only 6 of the 38 subjects cured, or subsequent clinical observation and examination of the faeces. The author says that *T. saginata* requires at least two months for its regeneration before eggs can again be laid. Clinical and parasitological observation of the 32 subjects in whom the head was not found showed that cures lasted for periods varying from more than three months (two subjects) to more than six months (seven subjects) more than one year (five subjects) more than two years (five subjects) and more than three years (13 subjects). The tapeworms passed were coloured an intense yellow by the acranil. The age of the subjects varied from 3 to 60 years 19 were males and 19 females. The author suggests administration of acranil by means of a duodenal sound to avoid the symptoms of intolerance. [The author gives the formula as the hydrochloride of chloromethoxyacridylammodiethylammonopropanol. It has been given (this *Bulletin* 1943 v 40 439) as 3-chloro-7-methoxy-6-diethylamino-5-hydroxy-propylammonium acridine dihydrochloride.]

The author quotes the experience of two other workers with this drug in *T. saginata* infestation

G. Lapage

RIVAS, C. I. GÓMEZ, E. & MANTILLA, L. R. Estadística de la hidatidosis en el Instituto de Clínica Quirúrgica. [Statistics of Hydatid Disease in the Institute of Clinical Surgery.] *Boletín Inst. Clin. Quirúrg.* Buenos Aires, 1944 Nov-Dec v 20 No 168, 845-53.

— — — & — — — Consideraciones sobre la estadística de la hidatidosis en el Instituto de Clínica Quirúrgica. [Considerations on the Statistics of Hydatid Disease in the Institute of Clinical Surgery.] *Ibid.* 856-7.

The second of these two papers briefly summarizes the first. For details the latter itself must be consulted only its main conclusions can be given here. The authors analyse the records of cases of hydatid disease operated upon at the Institute of Clinical Surgery during the period April 12 1919 to December 1 1943 and compare these with similar reports published in 1922 and 1932. From 1919 to 1922 there were 85 cases (32 per year) from 1922 to 1932, 387 cases (39 per year) from 1932 to 1943, 263 cases (24 per year). In the latter period out of the 30,601 operations of all kinds done 748 (2·4 per cent.) were for hydatid. But many cases are now operated upon near their homes in centres established by the Institute's campaign against this grave disease. Among the 748 subjects 425 had liver cysts, and 153 lung cysts. The authors regard these as infestations conveyed by the venous route and they also include

in this category the 78 peritoneal cysts which are they think secondary to liver or splenic cysts (primary peritoneal hydatids being in their opinion exceptional) Thus 87.85 per cent of the 748 subjects were infested by the venous route and 12.15 per cent. by the arterial route these figures accord with figures which are the authors say accepted as average values namely 85 per cent by the venous and 15 per cent. by the arterial route During the period under review liver cysts have decreased from 63 per cent. in 1922 to 56 per cent in 1943 a fact which is also attributed to the campaign against the disease The mortality at or immediately after operation was 10.9 per cent in the report published in 1932 and is 12 per cent in the present report. The mortality of subjects with liver cysts was also 12 per cent that of subjects with lung cysts was 14.83 per cent and that of subjects with peritoneal cysts 15.38 per cent Clinical histories showed that 35 per cent of subjects with liver cysts had not shown symptoms for longer than six months while others had shown symptoms for periods varying from six months to more than 20 years. The commonest symptom was evidence of the presence of a tumour of the liver (in 80 per cent of subjects) while 68 per cent had liver pain (diffuse or colicky) and 18 per cent had jaundice The position of the cysts on the liver is discussed. Liver cysts co-existed with cysts elsewhere in 52 of the subjects most often in the peritoneum Similar figures are given for cysts in the lungs peritoneum, spleen kidneys bones abdominal and thoracic body walls muscles and other sites The surgical technique adopted for treatment is described. [In the same issue of this *Journal* (p. 838) Rivas discusses more fully the surgical treatment of hydatid cysts of the liver.] Mortality can be but little affected by improvement in treatment prophylaxis alone is useful until biological treatment [presumably the biological treatment of CALCAGNO (1939) *Boletines y trabajos de la Acad. Argent. de Ciruj.*] based on the increase of heterophilous antibodies after injection of hydatid fluid into subjects with hydatid cysts (see also GRAÑA this *Bulletin* 1944 v 41 764)] can be developed sufficiently to replace surgery

G Lapage

EINHORN N H MILLER J F & WHITTIER L. Intestinal Polyparasitism
Clinical Survey of One Hundred and Sixty-One Cases of Infection with
Multiple Intestinal Parasites in Children *Amer J Dis Children* 1945
June v 69 No 6 350-58

This is an account of one of five surveys of 516 children in Gorgas Hospital Ancon Panama Canal Zone made during 1941 1942 and 1943 they were infested with one or more of five species of intestinal nematodes—*Ascaris lumbricoides* *Enterobius vermicularis* hookworm *Trichuris trichiura* and *Strongyloides stercoralis*. Of these 357 were infested with single species, and 161 had more than one species the former group has been separately reported on [this *Bulletin* 1945 v 42 578 and below] and the present paper refers to the latter group

Of the 161 children 116 lived on farms or in rural communities with primitive living conditions and no sanitation 130 were of mixed race and 29 were negroes Their ages ranged from 9 months to 12 years and only six were under two years.

As most of the patients were admitted for other diseases it was difficult to relate symptoms and some laboratory findings to the presence of the worms it was found however that eosinophilia above 4 per cent. occurred in 30 (18.6 per cent) only and in 14 of 42 who had no other disease besides helminthiasis

In treatment hexylresorcinol was the safest most efficient and easiest to administer of the vermifuges used tetrachlorethylene was most effective for hookworm infestation and gentian violet in enteric-coated tablets was effective

EINHORN \ H. MILLER J F & WHITTIER, L. Ascariasis Clinical Survey of One Hundred and Twenty Five Cases of Infection with *Ascaris lumbricoides* in Children. *Amer J Dis Children* 1945 Apr v 69 No 4 237-46 2 figs.

The authors studied 125 subjects aged between 11 months and 12 years in the Gorgas Hospital, Ancon, Panama Canal Zone from Jan. 1 1941 until Jan 1 1944. Co-existing infestations with other nematodes were frequent, but these are excluded from this report. All socio-economic groups are represented among the subjects. 5.6 per cent were whites 36.8 per cent. negroes and 57.6 per cent mestizos (half castes) (most of whom literally lived "on the soil"). Government communities with minimal overcrowding and excellent sanitation provided 12 per cent. of the subjects. the cities Colón and City of Panama (in the centre of which there is overcrowding but good sanitation not fully used and on the outskirts bad sanitation and no street paving) provided 26.4 per cent of the subjects (this degree of infestation was not expected from these areas but it is suggested that these subjects lived in areas of poor sanitation or moved often to such areas from areas of good sanitation or that the addresses given were those of the fathers who lived in areas of good sanitation on account of their work while the families lived in rural areas). rural and semi-rural communities with no sanitation provided 61.6 per cent. of the subjects.

A high incidence in early life is shown by the fact that one girl aged 11 months died of a heavy infestation (see below) (this subject must have been infested at the age of 9 months or earlier). 16.8 per cent were infested before 18 months and 52.8 per cent before four years. The boys numbered 54.4 per cent. and the girls 45.6 per cent. The authors emphasize the fact that 79.2 per cent of the subjects were brought to hospital because of diseases other than ascariasis and that in most of the subjects the ascariasis caused either no symptoms or only unimportant ones. these were worse in the younger children. Only 26 (20.6 per cent) had symptoms due to ascariasis alone. The commonest co-existing disease was malaria (in 55.2 per cent of subjects). respiratory infections were the next commonest (in 16 per cent). The most frequent symptoms considered to be due to ascariasis were vomiting (in 22.4 per cent. among whom 10.4 per cent vomited *Ascaris*) and the passage of *Ascaris* by the bowel (in 22.4 per cent). Malnutrition was frequent. Other symptoms were abdominal pain (in 8 per cent) anorexia (in 8.8 per cent) diarrhoea (in 8.8 per cent) abdominal distension in two subjects (ascribed to the tuberculous present as well) and excessive appetite in one subject. There was cough in 5.6 per cent and fever in 11.2 per cent and some bronchopneumonia and lobar pneumonia but it is suggested that these were not due to migration of *Ascaris* larvae. chest signs were rare and no larvae were found in the sputum. The pallor circles under the eyes poor development and mental and physical sluggishness mentioned by other authors as symptoms of ascariasis were not noticed. The authors conclude from their blood examinations and comparison of these with those of 30 children without ascariasis (the results of which were the same) that the subjects with ascariasis were not anæmic, that the number of their white blood cells was normal for this area and that eosinophilia (noted in only 11.2 per cent. of the subjects) was no index of the severity of the infestation. The stools of all subjects contained eggs of *Ascaris*.

Eight subjects were treated with oil of chenopodium in doses (not specified) reckoned according to the age and preceded and followed by a magnesium citrate purge. Chenopodium failed in two subjects, who were then given hexylresorcinol. Tetrachlorethylene was given to 15 subjects but was not effective. Hexylresorcinol was given to 86 subjects in doses of 0.1 to 0.2 gm.

in gelatin capsules (0.1 gm. per year of apparent age) preceded by magnesium citrate on the previous day and followed 24 hours after the hexylresorcinol by the same purge and in severe infestations by an enema also. Two courses of hexylresorcinol were given to 11 subjects and three to two subjects. Infrequent vomiting was the only sign of intolerance. After the vermifuge signs of toxæmia (weakness lassitude anorexia) due to absorption of products of the decomposition of the nematodes were often noted. Hexylresorcinol seemed to be the safest and most effective anthelmintic of the three used and the easiest to give. Capsules can be put directly into the oesophagus of young subjects. Its general results were all that could be desired: it does not affect the migratory larvae but it gave the children a new lease of life. Reinfestation is likely but as they grow older the children seem to suffer less. There can be no adequate therapy until sanitation prevents reinfestation.

Autopsies upon four subjects who died are described in detail. In two of these *Ascaris* was incidental to the primary cause of death. In the other two death was due to the *Ascaris* infestation. In one of these subjects aged 2 years one *Ascaris* was found in the oesophagus four in the stomach 79 in the small and large intestine: an *Ascaris* was protruding from the perforated appendix (yet of all the appendices removed from children during the period covered by this report none contained *Ascaris*): there was generalized peritonitis with ascarids in the peritoneal cavity diaphragmatic pleurisy and dehydration and emaciation. In the other child, aged 11 months there were groups of coiled *Ascaris* larvae in both mastoid antra but without purulent exudate: the right tympanic membrane was perforated. The brain was normal. In the liver there were numerous ascarids in the biliary tract and ducts and in the parenchyma (in cysts with brownish-green necrotic walls containing one to eight parasites which measured 2 to 4 cm. long): it was estimated that there were 150 parasites in the liver. In the gall bladder which contained no bile or mucus there were 40 ascarids (the longest measuring 10 cm.). Two ascarids were found in the pancreas one of which protruded from the main pancreatic duct into the duodenum. In the oesophagus there were three ascarids in the stomach 20 in the duodenum 38 and in the small intestine 181—a total of 242: ulceration and other lesions were absent. The histology of the brain liver and other organs is described. *G. Lapage*

SARTORIUS K. Intestinal Obstruction due to Round Worms (*Ascaris lumbricoides*) with a Report on Two Cases. *Clin. Proc. Cape Town* 1945 June, v 4 No. 4 194-9

CLEARKIN P. A. A Note on the Laboratory Diagnosis of Filariasis, resulting from Infection by *Wuchereria bancrofti*. *Caribbean Med. J.* 1944 v 6 No 5 317-21

Referring to earlier work upon skin tests and precipitin and complement fixation reactions for the diagnosis of infestations with filariasis the author says that the skin test has been used as a routine measure for the last 2½ years at the Central Medical Laboratory Georgetown British Guiana: this paper records the results. [See also Clearkin this *Bulletin* 1944 v 41 598.] The antigen was made from *Dirofilaria immitis* obtained from unwanted dogs by the method here described by the author. The routine now adopted is to try first a 0.2 per cent. extract and if the test is negative to try a 0.5 per cent. extract. This procedure detects the less sensitive subjects who may give negative reactions with extracts weaker than 0.2 per cent. An appreciable number of subjects are phenol-sensitive so that controls done with the 0.5 per cent. phenol in 0.85 per cent. saline with which the extract is made are important.

Mosquito	Dissected on death before 17th day after feeding		Dissected alive on 17th day after feeding	
	Infected	Not infected	Infected	Not infected
<i>Culex erythrorhoxus</i>	14	11	18*	12
<i>C quinquefasciatus</i> (<i>C fatigans</i>)	4	2	17†	3
<i>C tarsalis</i>	0	0	1‡	2
<i>Aedes (Sticticus) taeniorhynchus</i>	10	28	0	4
<i>Anopheles maculipennis f. freeborni</i>	0	1	0	6
<i>A. pseudopunctipennis</i>	0	1	0	0

8 had larvae in the proboscis † 13 had larvae in the proboscis
1 had larvae in the proboscis

Culex stigmatosoma, *Culiseta inornata* and *Culiseta incidens* refused to feed, and only one specimen of *Anopheles pseudopunctipennis* fed.

The authors conclude that *Culex quinquefasciatus* (*C fatigans*), *C erythrorhoxus* and probably *C tarsalis* would be vectors of the disease if persons with microfilariae in their blood were present in South California. J. F. Corson

HU S. M. K. Studies on the Susceptibility of Shanghai Mosquitoes to Experimental Infection with *Microfilaria malaysi* Brug. VII. *Culex fuscans* Wiedemann. Chinese Med J Washington. 1944 July Sept., v 62, No 3 255-9

1 The susceptibility of *Culex fuscans* to infection with *Microfilaria malaysi* has been confirmed.

2 Of 68 *Culex fuscans* fed on two cases of *Microfilaria malaysi* infection, 2 or 2-9 per cent. were found with mature filarial larvae in them.

3 Fourteen of the mosquitoes were found with only dead encapsulated microfilarial form larvae while the remaining 53 mosquitoes were negative for any filarial larva.

4 *Culex fuscans* is not likely to play a significant role in the transmission of *Microfilaria malaysi* infection in the lower Yangtze region because in this part of the country it seldom enters houses or feeds on man."

JAFFE H. L. Evaluation of Roentgen Therapy in Filariasis. Amer J Roentgenol & Rad Therapy 1945 May v 53 483. [Summary taken from J Amer Med Ass 1945 Aug 4 v 128 No 14 1049]

Jaffe evaluates the results of roentgen therapy in filariasis by comparing the course of the disease in a group of 50 patients treated by roentgen rays with that of an untreated group of the same number. Three months after treatment the course of filariasis was similar in the irradiated and in the untreated patients. Several patients derived benefit from roentgen therapy in that some glandular swellings were reduced in size and were rendered less painful. No harmful effects were observed as a result of this roentgen treatment. Total body irradiation offers no advantage over local roentgen therapy and at times does not appear to be as effective in relieving the pain of enlarged glands or in reducing their size. Roentgen therapy did not influence the frequency, duration or severity of recurrent attacks after periods of remission. Several patients who complained of a pleuritic type of pain presented lesions of a

transitory and migrating type of chronic pneumonitis affecting one or both lungs. These patients were afebrile and showed a normal white blood cell count.

WAR MEDICINE Chicago 1945 June v 7 No 6 377-84 2 figs. *Filaria* (*Wuchereria*) with special reference to Early Stages War Department Technical Bulletin TB Med 142

VARGAS L. Notas sobre la oncocerciasis. I Consideraciones sobre la población de simúlidos adultos. [Notes on Onchocerciasis. I. Considerations on Adult Simuliid Populations.] *Rev Inst Salubridad y Enfermedades Trop Mexico* 1945 Mar v 6 No 1 51-9 English summary

Data concerning the black fly population are necessary to understand the epidemiological facts in onchocerciasis. Data obtained by the use of light traps are analysed as well as those reached by the use of capture on human baits. To get better information on the problem of the population it is recommended to test human baited traps.

VARGAS L. Notas sobre la oncocerciasis. II El factor luz y los simúlidos Adultos [Notes on Onchocerciasis. II. The Effect of Light on Adult Simuliidae.] *Rev Inst Salubridad y Enfermedades Trop Mexico* 1945 Mar v 6 No 1 61-6 English summary

The black flies are strongly phototropic positive. Ultraviolet light attracts them remarkably, on the contrary red light or darkness makes them motionless. We applied this observation maintaining females without any other food up to six days but as in nature the females looking for blood have already been fertilized at the end of this period they show mature eggs and as they are unable to lay them in captivity die in the 5th or 6th day after the blood meal. For the study of the transmission of nemathelminthes or protozoa by black flies the preservation of females in the dark may be useful.

VARGAS L. Notas sobre la oncocerciasis. III Algunos factores que afectan la fijación de las larvas de simúlidos [Notes on Onchocerciasis. III Factors affecting the Fixation of Larvae of Simuliidae.] *Rev Inst Salubridad y Enfermedades Trop Mexico* 1945 Mar v 6 No 1 67-70 English summary

Larvae of the black flies *S. metallicum* and *S. callidum* are easily dislodged from their breedings by swift running waters or by water carrying fine debris, grains of gravel etc. Larvae fixed in the lower surface of leaves etc. are better protected and are more apt to remain there.

MUKERJI A K & BHADURI N V. Gnathostome Infection of the Eye. *Indian Med Gaz* 1945 Mar v 80 No 3 126-8 2 figs (1 on pl.) [10 refs.]

Full-grown adults and larvae of *Gnathostoma* have been recorded from man since 1889. Up to 1934 a total of 21 cases have been listed [see PROMMAS and DAENGSVANG this *Bulletin* 1934 v 81 801] and during the last ten years three more. Two of these latter were from Bengal (from which province three cases were previously known) and one was from Siam. In India human gnathostomatosis is known so far only in Bengal. In the earlier Bengal cases the worms were found in cutaneous nodes, superficial tumours and breast

abscesses in the Siamese case the worm was found in an abdominal tumour removed surgically. The case here reported is the sixth from Bengal and is the first in which the worm has been found in the eye.

The subject was a Hindu male aged 26 who had never been out of Bengal and had never eaten raw or dried fish although he had bathed in a tank. Before coming to hospital he complained of a dull ache in the left side of the nose extending to the left frontal region, followed by swelling of the left cheek and left lower eyelid extending up to the roots of the hair so that the left eye could not be opened. Orbital cellulitis was found but vision was at first normal. Two days later only movements of the hand were recognized and there were haemorrhages in the retina and vitreous humour. Three days later there was severe iritis with small grey nodules on the iris. These nodules disappeared, but later iritis reappeared with one large grey nodule on the iris and also a pigmented nodule. Both these disappeared and later another pigmented nodule appeared which was seen to move. The next day wavy movements were seen in it and the worm was removed from the angle of the anterior chamber of the eye. The eye quickly became normal again.

The worm was 3 to 5 mm long by 0.41 mm at its broadest (about its middle). The head bulb was 0.116 mm long by 0.25 mm broad. On the head bulb there were four rows of spines, with 40 spines in each row. Spines continued back on the transverse ridges on the body to the extreme posterior end of the worm, becoming gradually smaller from before backwards. There were four cervical sacs in the oesophageal region but no genitalia were seen. The worm most resembled the one described by MAPLESTONE (this Bulletin 1930 v 27 834). Because the spines continued almost to the posterior end the authors do not think this was an immature specimen of *G. springerum*. It was probably not *G. hispidum* because the head spines were not simple. They are inclined to think it was a specimen of the new species described by Maplestone [loc cit].

In man both larvae and adults have been found so that man can be an accidental definitive host. The natural hosts are the cat and the dog. No adult worm has yet been found in fish but man is probably infested by eating infested *Cyclops* or fish. In Bengal, infestation by eating fish is not likely because fish are always cooked there and dried fish is not usually eaten raw. There is as yet no proof that the larvae acquired by man ever become mature in him. Because man is an unsuitable host the worm wanders in him and causes symptoms.

G. Lapage

PETERSEN, M. C. & FAHEY, J. Oxyuriasis. Simplified Method of Diagnosis with Glass Slide. Incidence in a Minnesota State Hospital. Result of Treatment with Gentian Violet. *J. Lab. & Clin. Med.* 1945 Mar v 30 No 3 258-61.

At Willmar State Hospital, Minnesota, the authors noted 4 per cent. of eosinophils in differential white blood cell counts and a routine search usually revealed *Enterobius*. A survey of the whole institution was therefore undertaken between September 1940 and July 1942. The institution is built on the cottage plan. Each cottage accommodates about 100 subjects and frequent transfers of patients from one cottage to another occur. The total capacity of the cottages is 1450 beds. The majority of the patients are chronic mental cases transferred from other hospitals. Most of these have been in hospital more than a year and many more than ten years. A minority of patients are drug-addicts and alcoholics admitted directly and remaining for only two to four months.

The authors first used the NIH swab [HALL this *Bulletin* 1937 \ 34 878] They then tried the cellophane tape used by JACOBS (*J Pediatrics* 1942 \ 21 497) this was as efficient as the NIH swab but was too slow They then used glass slides with smooth edges and found these as accurate and much faster than the NIH swab or the cellophane tape At one end of the slide a number was scratched or etched for identification of the slide and of its exposed side. Slides were put in metal holders so that they did not touch each other They were cleaned and used repeatedly Subjects were examined between midnight and 4 a.m. and no baths were allowed the night before examination. The subject was asked to bend over and to strain slightly The examiner would hold the marked end of the slide and press the other end against the anal mucosa and muco-cutaneous junction in such a manner that one edge of the slide would be toward the centre of the anus The slide would then be lifted and the opposite edge pressed against the opposite anal margin Only the marked side of the slide was exposed The moisture of the anal margin was enough to make the eggs of *Enterobius* adhere The eggs were usually found along the edges of the slide Slides could be kept several days before examination All patients in each cottage were examined the same night Subjects who were negative were re-examined until all other subjects were negative sometimes 18 such examination were made Fairly frequently the authors found large numbers of eggs on slides from subjects who had been previously repeatedly free from eggs

In all 1,871 subjects were examined Of these 1 100 (59 per cent) were infested 72 per cent of chronic mental subjects and 1 per cent of mebrates were infested but none of the employees although two employees had previously been treated for enterobiasis A table gives the incidence It shows a decidedly higher incidence among males (e.g. 11 per cent of 83 female persons in cottage 3 88 per cent of 103 males in cottage 4 40 per cent of 100 females in cottage 5 and 95 per cent of 106 males in cottage 6) The incidence was highest among the disturbed and deteriorated subjects it was lower among subjects received by transfer from other hospitals perhaps because they had not been so long in hospital as the others.

All the infested subjects were treated with gentian violet Two enteric coated tablets each containing half a grain (0.032 gm) of gentian violet were given by the mouth twice a day after meals for eight days after a rest of eight days this course was repeated after a second rest for eight days a third course was given A total of 48 grams (31 gm) was thus given over 40 days Toxic symptoms were rare in males but fairly frequent in females Some subjects lost weight during treatment others showed anorexia, nausea vomiting mild abdominal pain and diarrhoea. The symptoms disappeared when treatment was discontinued for a few days and the treatment was then resumed. To test the efficacy of gentian violet six examinations were made during four weeks After the first course of gentian violet eggs of *Enterobius* were found in 88 (9 per cent. of subjects infested before treatment began) after the second course they were found in 11 (1 per cent) and after the third course in 2 (0.2 per cent.) One subject was passing eggs after five courses. In two cottages 208 subjects were examined ten months after treatment Of these 31 (29 per cent.) in cottage 6 and 46 (45 per cent) in cottage 12 (i.e. 37 per cent of 208 subjects) were then found to be infested.

(For a summary of the long series of studies of enterobiasis in the United States on the diagnosis and treatment (with gentian violet hexylresorcinol tetrachlorethylene and santonin) of enterobiasis see CRAM this *Bulletin* 1943 \ 40 618 for treatment with phenothiazine see SISK *ibid* 927 BERCOVITZ, *et al* *ibid* 929 MOST *ibid* 930 and the bibliography appended to the last named abstract. MILLER and ALLEN *ibid* 1942 \ 39 781 compared the

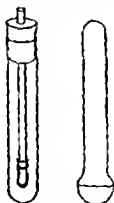
effects on *Enterobius* of phenothiazine and gentian violet. In the abstract quoted the dose of gentian violet given by these authors was given in error (see this *Bulletin* 1944, v 41 306) in grammes instead of grains. For some references to the diagnosis of enterobiasis see the two abstracts next following below].

G. Lapage.

SCHLUTTER W & SWELLENGREEL N H Eine zweistufige Methode zum Nachweis von Oxyuris-Eiern Ihre Leistung gegenüber dem amerikanischen NIH Wischer [A Two-Stage Method for the Detection of Oxyuris Eggs. Its Efficacy compared with that of the American NIH Swab. *Zent f Bak I Abt Orig* 1943 Dec. 11 v 151 No. 1 71-80 3 figs. 11 refs.]

The authors worked in Amsterdam. They found that after the perianal skin had been given a brief wash with water 99 per cent. of the *Enterobius* eggs on it were washed off and only 1 per cent. could be recovered from within the anal sphincter although they found eggs adhering to the surface of formed stools. When a subject who had an average of 400 eggs (in six preparations) on the perianal skin was washed, an average of 0.25 per cent. of the eggs were recovered. This result was not expected, because the stickiness of *Enterobius* eggs is always so much emphasized in the literature but it suggests that simple washing can be an effective means of control of the spread of *Enterobius*. Observation of the process of egg laying by *Enterobius* showed that the eggs are laid in a stream—a dense cluster is laid in a few minutes and movement of the nematode during egg laying which precedes the death of the female is feeble so that the eggs are not widely distributed by the nematode. The whole contents of the uterus are laid—the authors quote literature which indicates that some ten to thirteen thousand eggs are deposited. The eggs are laid in clusters (photographs of these are given).

With the implements generally used—match stalks, the cotton wool swab of HEBBER (*Jakob's Kinderkalk* 1922, v 96 1) the scraper of JAFFA [this *Bulletin* 1925 v 22 491 and the NIH swab of HALL (this *Bulletin* 1937 v 34 879) only a part of the perianal skin is wiped or scraped and it



NIH Cellulose Swab (left) and Glass Pencil (right) for detecting *Enterobius* Eggs. 1 actual size

Reproduced from *Zent f Bak I Abt Orig* 1943 Dec. 11

depends on chance whether eggs are taken up or not especially when infestations are light. To avoid this source of error the authors tried the method of breaking up the egg clusters and distributing them over the perianal skin.

First they massaged this skin with the finger and water for 10-15 seconds thus making an emulsion containing squamous cells mucus sweat and faecal matter. Examinations of this emulsion being favourable they then used for the same purpose a glass pestle made from 10 cm. of thick walled glass tubing the end of which was blown into a globe about 1½ cm in diameter the lower half of this globe was ground rough so that it could exert sufficient friction to dislodge material between the perianal folds and on the perianal skin (stage 1). The pestle was moistened with water before use and the emulsion made with it was transferred to a drop of water on a slide and examined under a cover glass (stage 2). The emulsion can also be spread over a slide and dried and then is more readily transportable than the NIH swab.

The effects of drying on the eggs must be considered. When one such dried drop was incubated at 37°C in pepsin solution for some hours larvae emerged from the eggs in it after eight days and six weeks after eight weeks this happened only in some eggs and after 13 weeks only in isolated eggs (cf HELLER this *Bulletin* 1945 v 42 579 who found that sensitivity of the eggs to drying depends upon the stage of development of the embryo and on its cuticular covering and concluded that drying and ventilation of rooms will kill most of the eggs and reduce the degree of infestations). By this method of drying drops eggs in dust were found to be viable (but see also the following abstract). These dried drops can be examined by wetting them again with water or dilute NaOH but examination in cedarwood oil is the method of choice for *Enterobius* eggs although it is not satisfactory for the eggs of *Incylostoma* because faecal smears are thicker than these dried drops and are not cleared sufficiently by the oil. It is better to ring the dried drops with ink so that they can be located after they are cleared. The eggs are not cleared and look rather like air bubbles. Drops thus cleared remain unchanged for weeks. Liquid paraffin can also be used it is less effective but is cheaper and easier to clean off.

Tests of this method showed that when the emulsion samples taken with the pestle were examined in water the first drop taken contained about one third of all the eggs on the pestle and the second drop about the same or even a larger number. When drops were taken one after another (the pestle being washed after each was put on a slide and then recharged with emulsion, so that two-thirds of the eggs taken up each time were lost) the drops were negative after 30 such samples had been taken. In spite of the washing of the pestle the numbers of eggs in the first six drops were not greatly different although the size of the drops was judged only by the naked eye so that their contents were not strictly comparable.

The authors claim that this method requires only about one third or less of the time taken by the NIH swab. They examined 50 subjects with the NIH swab in 578 minutes (about 9 hours) and the same 50 in 172 minutes by the pestle (about 3 hours). This included the counting of the eggs, which is not necessary for diagnosis. They claim that the NIH swab takes three to six times as long as the pestle does when the number of eggs present is constant. Samples taken from negative subjects must be searched throughout their extent but in 37 examinations the time taken to do this was 11 minutes with the NIH swab and 2½ minutes with the pestle drops. The watery medium used to examine the NIH cellophane swabs takes longer to examine and oil cannot clear cellophane.

Whatever instruments are used they must be cleaned after each examination. The authors think that the directions for cleaning the NIH swab and its containers [FOLAN this *Bulletin* 1940 v 37 300] are excessively stringent. Cleansing of the pestle is very simple. Experiments showed that washing is enough because the finely-ground emulsion which has not dried on the pestle

adheres only feebly to the glass. The authors scour the pestle head and then repeat this in a vessel containing "strong disinfectant" and a cotton-wool pad on which the pestle is left standing until its turn for use comes round again. They always used two pestles.

Tables give the results obtained with the pestle and the NIH swab.

For the examination of 50 subjects the NIH swab was always used first: this gave it an advantage. Yet with it only 37 of the 50 subjects were positive while all 50 were positive with the pestle. In addition the pestle recovered nearly four times as many eggs (3,372 as compared with 831). Examination of one subject showed, however, that the NIH swab recovered more eggs than the pestle in the proportion of 201 to 2 (cf. one similar instance in the succeeding abstract below). Probably the NIH swab in this instance chanced to take up most of the eggs deposited in clusters. When 12 children were examined first with the NIH swab and then after making an emulsion on the perianal skin with the pestle the first eight were negative at the first examination with the NIH swab while only two of these were negative with the pestle so that the pestle reduced the number of re-examinations required. The pestle also recovered more eggs from these children. The authors claim that the pestle detects eggs when the infestation is so light that the NIH swab fails to do so. Its use does not exclude the necessity for re-examinations, but fewer than the seven to ten re-examinations recommended by those who have used the NIH swab are necessary. The authors showed that when schoolchildren take baths only once a week the eggs adhere to them all the week until the bath removes them. The pestle is simpler to clean and to manage and the slides and covers are more easily put back into use. It does not rasp or scratch the skin, whereas the sharp cellophane folds of the NIH swab may do this.

G. LaPage

SCHIFFNER, W. & SWELLENGREBEL, N. H. Der Nachweis von Oxyuren-Eiern am After im Nagelschmutz und im Zimmerstaub. II Mitteilung. [On the Detection of Oxyuris Eggs on the Perianal Region, in the Nail-Dirt and in the Dust of Rooms. *Zent. f. Bakt. I Abt. Orig.* 1944 Jan. 28 v. 151 No. 2, 114-22, 1 fig.]

In this paper the authors give further evidence which demonstrates in their opinion, the superiority of the pestle devised by them (above) over the NIH swab.

Five children were examined first with the NIH swab and all were negative. Then they were examined with the pestle and all were found to be positive (28 eggs found). A third examination of them with the NIH swab which now operated on the faecal emulsion made for the pestle detected three positives (four eggs found). The authors claim that this indicates that the preparation of the faecal emulsion, which breaks up the egg clusters and distributes the eggs more uniformly over the perianal skin, improves the performance of the NIH swab.

When 13 other children were examined by the same method, all were positive at all three examinations, but the second NIH swab recovered far fewer eggs than the pestle (first NIH swab 483 eggs, pestle 3,672 eggs, second NIH swab 800 eggs). Examination of 4 other children revealed no special advantage of the pestle. When, however, two other children were later examined in the same way the first NIH swab recovered more eggs than the pestle (cf. the similar instance in the abstract immediately above). Examination of 123 children, aged 2 to 4 years with the pestle showed that 81 per cent. were positive. Studying the numbers of positives recorded after successive examinations the authors found that 89 per cent. of 148 children aged 5-8 years were positive.

at the fourth successive daily examination and they compare this result with the record of SAWITZ *et al* [this *Bulletin* 1940 v 37 82] who found that 88 per cent. of 131 children aged 6-14 years bearing an infestation similar in degree to that studied by Schuffner and Swellengrebel were positive at the fourth examination [with the NIH swab] at intervals of one to two days.

Discussing the number of eggs to be found in the finger nail-dirt the authors quote WILHELM and QUAST [this *Bulletin* 1925 v 22 884] who found *Enterobius* eggs in the nail-dirt of 60.4 per cent of the children examined a figure which was near the actual incidence of the infestation in these children. Wilhelm and Quast therefore suggested that examination of nail-dirt could replace examination of the perianal region. Schuffner and Swellengrebel found however that examination of the nail-dirt detected little more than one third of the actual infestation (95 per cent) in the children whom they examined and that to obtain this figure three examinations were required. Examination of nail-dirt cannot therefore replace examination of the perianal region—not at least in Amsterdam where children are mostly protected at night by pyjamas. But study of the nail-dirt has epidemiological value although repeated examinations of it are necessary. The authors like Wilhelm and Quast moistened the finger nail region in 1 per cent NaOH but then removed the nail dirt with match-stalks or with a nail-cleaner (not with the cotton wool used by Wilhelm and Quast to which an unknown number of eggs may adhere) and put it all in a drop of water on a slide after drying it was examined in cedarwood oil or liquid paraffin. The authors concluded that the ring finger can be ignored without detriment to the results.

Some of the literature on the distribution of the eggs in house-dust is discussed. The authors obtained poor results with the method of NOLAN and REARDON [this *Bulletin* 1939 v 36 845] who obtained samples of dust with a moist brush and examined them in 1 per cent NaOH. The authors preferred a floatation method. Dust was either swept up or obtained with a moist brush and filtered through phosphor bronze gauze with a mesh of about 70 microns. Eggs in it were then floated up in solutions of either NaCl (sp gr 1.13) zinc sulphate (sp gr 1.33) or zinc chloride (sp gr 1.7). The authors preferred zinc chloride but the heavier salts bring up detritus which may obscure the eggs (see literature referred to below). Eggs were floated up in small tubes or cylinders with a cover-glass on the top. The authors are convinced that no eggs are lost by removal of this cover for examination. They watched the rise and fall of the eggs in the solutions used. Some eggs may adhere to the sides of the floatation cylinders others may adhere to heavy particles which sink and draw the eggs to the bottom. The use of the glass cover is better than the wire loop recommended by HOFMANN and BARBER [this *Bulletin* 1919 v 13 219]. In zinc chloride (sp gr 1.7) the eggs rose at a rate of 1 mm in 45 seconds. In water they sank at a rate of 1 mm in 15 seconds. To obtain all eggs the cover must remain on for $\frac{1}{2}$ hour. Eggs eventually sink again but were still at the top after 48 hours. SCHUCHMANN and KIEFFER (*Berlin Tierärz. Woch.* 1922, p 220) used sodium waterglass 1 part water 2 parts for floatation and claimed results similar to those obtained with $ZnSO_4$. Schuffner and Swellengrebel working with 1 part of water glass to 1 part of water found it troublesome to use and less efficient than NaCl. It also spoils glassware. They also tried potassium lactate (sp. gr 1.33) potassium acetate (sp gr 1.26) and calcium chloride (sp gr 1.25) but all these were inferior. The specific gravity is therefore not the only factor concerned.

Tables give the numbers of eggs obtained from the dust of various parts of schools in Amsterdam. An astounding number of eggs was recovered from the dust of closets where the dust had been undisturbed for weeks on

the window fastenings large numbers were also found in the dining rooms in which the children remained for only a short time. The authors concluded that the height of the surface from which dust is taken (e.g. the top of a table or high cupboard) has no significance because the eggs are blown about everywhere. Most of the eggs found in dust seemed, however to be empty. Some hatched out embryos but the author were not convinced that eggs found in dust can develop into adult worms after they have been swallowed. HELLER [this *Bulletin* 1945 v 42 578] quotes the conclusion of VOLAN and REARDON [loc. cit.] that 90 per cent of eggs found in dust are not viable.

With reference to the three preceding abstracts the following references may be useful. MAZZOTTI and OSORIO (this *Bulletin* 1943 v 40 617) compare the results obtained with the Graham and the NIH swab. KUITUNKY ERBAUM (ibid 1942 v 39 780) compares the value of the NIH the Graham and the Frost cellophane swabs. VON HOFE (ibid 1944 v 41 958) describes his use of adhesive Scotch tape. PODYAPOLSKAYA (ibid 1944 v 41 301) refers to the wide use in Russia of the examination of scrapings of the perianal skin for the diagnosis of enterobiasis and adapts it to the detection of eggs of *Taenia*. MAZZOTTI (ibid 1945 v 42 134 398) also applies it to the detection of eggs of *Taenia*.

For further discussions of methods of floating up eggs of various species of nematodes and for reference to the vast literature on this subject, see the following abstracts. GORDON and WHITLOCK (1939 *J. Couns. for Sci. and Ind. Res. Australia* v 12 50) who describe their egg-counting slide for use with saturated solutions of NaCl which avoids most of the difficulties discussed by Schuffner and Swellengrebel above and is now widely used. It is briefly compared with the slide devised by WILKINS (this *Bulletin* 1943 v 40 67). SAVITZ (this *Bulletin* 1942 v 39 771) discusses the buoyancy in NaCl and ZnSO₄ of the eggs of *Enterobius* and some other species of nematodes. KATZ (*Amer. J. Hyg.* 1941 v 2 83) compares the merits of NaCl sugar ZnSO₄ MgSO₄ and sodium nitrate. OTTO *et al.* (this *Bulletin* 1941 v 38 473) describe a simplified ZnSO₄ floatation method. FAUST *et al.* (ibid 1940 v 37 62) discuss the use of ZnSO₄. EIGENFELD and SCHLESINGER (ibid 1944 v 41 496) describe a floatation tube designed to facilitate collection of the top layer of fluid and LANE (ibid 1940 v 37 477) discusses his well known centrifugal floatation method.]

G. Lapage

MAZZOTTI L. Investigación sobre oxiurias en 1120 niños residentes en regiones tropicales de México. [Enterobius Infection in 1,120 Children in Tropical Mexico.] *Rev. Inst. Salubridad y Enfermedades Trop. Mexico*. 1945 Mar v 6 No 1 37-40. English summary (3 lines).

HARRELL, G. T. & HORNE, S. F. Trichinella Skin Tests in Tuberculosis Sanatoriums, Hospitals for Mental Diseases, and General Hospitals. A Comparison of the Results in Tuberculous and Non-tuberculous Patients. *Amer. J. Trop. Med.* 1945 Jan 25 No 1 51-8 2 figs.

This paper is reviewed in *Bulletin of Hygiene* 1945 20 469.

DEFICIENCY DISEASES

ELLINGER, P. & BENESCH, R. Nicotinamide Methochloride Elimination Tests on Normal and Nicotinamide-Deficient Persons. With a clinical addendum by S. W. HARDWICK. *Lancet* 1945 Aug 18 197-9 [33 refs.]

"The development of a satisfactory saturation test for the assessment of the nicotinamide or nicotinic acid state of the human body has proved difficult.

The authors after giving a most useful summary of the work of others in this field give details of elimination tests carried out on 12 patients believed on clinical grounds to be suffering from nicotinamide deficiencies with clinical case notes and on seven normal persons. They say: "It should be stressed that the work reported here is of a preliminary nature and that no general conclusions can be drawn before considerably more material has been collected. Subject to a number of qualifications they believe it can be stated with some confidence that the nicotinamide methochloride elimination test described can yield useful information on the nicotinamide status of the human organism."

All those interested must read the original paper

H S Stannus

CHU H I Kuo P T & CHANG K P. Blood and Urinary Nicotinic Acid in Normal Chinese, Pellagra and various Pathological Conditions. *Chinese Med J* Washington 1944 July-Sept. v 62 No 3 231-45 [45 refs.]

Hou H C & Dju M Y. Urinary Excretion of Nicotinic Acid among Normal Chinese, Pellagrins and other Patients. *Chinese Med J* Washington 1944 July-Sept. v 62 No 3 246-54

EARLE K V. Arriboflavinosis in Northern Peru. *J Trop Med & Hyg* 1945 Feb-Mar v 48 No 1 10-11 [13 refs.]

The author examined for indications of arriboflavinosis 403 patients in hospital (admitted for various conditions not necessarily connected with nutritional deficiency) in Peru. The manifestations (and the percentages in which they were found) were as follows:—Angular stomatitis 10.19 per cent. lingual alterations 5.1 per cent. naso-labial seborrhoea 12.77 per cent. seborrhoea of the ears 3.19 per cent. facial comedones 15.9 per cent. The rates were higher in pregnant or parturient than in non pregnant women. Associated avitaminoses were common and are tabulated. *Charles Wilcocks*

DERMATOLOGY AND FUNGUS DISEASES

VARELA G OLARTE J & CASTRO ESTRADA S. The Kahn Triple Quantitative Verification Technique in the Serology of Mal Del Pinto (Pinta). *J Lab & Clin Med* 1945 Mar v 30 No 3 270-72 [10 refs.]

There is an old saying that "the best things come in small parcels." This small article is of much importance, for it is an account most succinctly expressed of an intensive study to determine the value of the Kahn test in mal del pinto. Just upon 20 years ago MENK found that the sera of pinta patients in many cases gave a positive Wassermann reaction: he gave 74.5 per cent as the figure. Others have confirmed this and more recently in 1940 LEÓN Y BLANCO showed that in 87.5 per cent of cases with generalized disease the Wassermann, Kahn and Muller tests were positive and in the late stages as many as 97 per cent. [This author had found the Wassermann and Kahn reactions negative in the primary stage: see this *Bulletin* 1941 v 38 91.]

Kahn in 1912-3 developed his triple quantitative technique which he believed to be specific for syphilis. The present authors have tested this with sera from pinta patients after carrying out the standard Kahn test in each case. They used three quantitative procedures: viz serial dilutions with distilled water and dilutions with 0.9 per cent. and with 2.5 per cent saline and Difco antigen. The standard test was also carried out on the globulin

injection of morphine. Uretic crystals were treated in the same way but renal calculi were removed by operation.

J. F. Corson

TROPICAL ULCER

JARVIS J. F. Tropical Ulcer. *East African Med. J.* 1945 May 1 22
No 5 134-44

This is an account of an address and discussion at the local branch of the British Medical Association. It deals with the subject of tropical ulcer on general lines, the points being illustrated by the personal experience of the author and those who took part. He considers the aetiology, clinical features and the treatment, curative and prophylactic. The aetiology is still obscure and calls for intensive research, for in the absence of more exact knowledge of the cause treatment must be except on general lines, empirical and prophylaxis haphazard. It is observed that these ulcers tend to recur in epidemics that labourers in one locality may many of them, suffer whereas others in apparently the same circumstances have a low incidence and also that conditions remaining apparently unchanged these ulcers may be prevalent at one time uncommon at another. To ascribe the prevalence to "lack of tissue resistance" is merely throwing the inquiry one stage further back and adds nothing to knowledge.

Clinically the ulcer exhibits three stages—active spread, arrest, and repair healing being delayed by indolence due to constitutional disease or unsuitable treatment, or by epithelial exhaustion—a term applied by the author to retardation or cessation of epithelialization. In others the ulcer becomes chronic from strangulation of the blood supply by a fibrous barrier below the granulations, new skin readily breaking down. In others the necrotic process may spread deeper to tendon and bone with resultant deformity if not checked in time.

The principles of curative treatment are rest and improvement in diet—the former being attained by application of plaster of Paris with no niggard hand. Locally the need for cleansing the site and keeping it clean is duly stressed. Scraping is recommended by some practitioners for indolent ulcers or those which are chronic from fibrosis but the author favours excision—removal of the whole surface, the skin edges and the granulations—followed by application of zipp and plaster. Prophylaxis is on common sense lines, namely medical examination and selection of labour recruits, early treatment of minor injuries, improvement in diet and, where possible communal cooking because men "on their own" and away from their women-folk will not bother to get vegetables or to cook their meals properly. Camp supervisors should make frequent inspections to see to these matters.

H. Harold Scott

RAO M. V. R., COLAH R. B. M. & KALLE R. A. "Tropical Ulcer" in East Khandesh. Treatment with Sulphathiazole Cod-Liver Oil Paste. *Indian Med. Gaz.* 1945 Mar 1 80 No 3 123-30 4 figs on 1 pl.

Tropical ulcers were common among poorly nourished people in the East Khandesh district of the northern section of the Deccan tableland, Bombay Presidency. The authors treated 127 cases by the following method. The ulcer was thoroughly cleaned under general anaesthesia, mopped dry with

gauze and a fairly thick layer of a water-in-oil emulsion containing sulphathiazole and cod-liver oil was applied and covered with a gauze-covered pad of cotton wool impregnated with sulphanilamide.

The water-in-oil emulsion was prepared according to the formula used by DIKSHIT and GARDHAM [*Indian Med Gaz* 1945 v 80 121] it consisted of sulphathiazole 12 calcium oleate 2 beeswax 3 cod liver oil 60 and water 40 parts. This dressing changed about every three days was continued until the ulcer showed healthy granulation tissue and was then replaced by 2 per cent solution of oxalic acid.

Small ulcers were almost healed within three weeks. General treatment consisted of rest in bed supply of good food shark liver oil, and fresh lime juice.

J. F. Corson

MOUSTARDIER G & NICOL R. Notes sur le traitement des ulcères phagédéniques [Notes on the Treatment of Phagedenic Ulcer] *Rev Sci Méd Pharm et l'Ét de l'Afrique Française Libre* 1943 Oct v 2 No 4 371-6

In 1930 Moustardier began to try intravenous injections of tartar emetic for patients with phagedenic ulcer in Indo-China with good results. Nine years later at Brazzaville he tried nitrosyl a vitaminized ointment and again the results proved to be very satisfactory. The authors have been using a combination of these forms of treatment. For adults they inject 1 cc. of 1 per cent tartar emetic two days later 3 cc. on the fifth day 5 cc. on the seventh day 10 cc. and thereafter 10 cc. on alternate days till the ulcer clears or cicatrizes but never exceeding a total of 12 gm. As soon as the ulcer is clean usually after the fourth or fifth injection they apply locally every 48 hours an ointment of cod liver oil and sepiolux (the composition of this is not given) until healing is complete.

In a table the authors give a list of 43 patients treated thus in hospital and eight treated as out-patients. In this table are stated the name sex and age the site and size of the ulcers the amount of tartar emetic injected and the length of time before the ulcer healed. The shortest time was six days the patient a man of 24 years with an ulcer 2 x 1 cm. on the left leg the longest 68 days a boy of 11 years with an ulcer over the tendo Achillis 2 x 2 cm. in another patient a man of 28 years an ulcer of 9 x 9 cm. over the same site as the last healed in 39 days and in a fourth a man of 28 years, an ulcer 5 x 4 cm. on the left leg was healed in 10 days. In every case the organisms found were a spirillum and fusiform bacillus. Generally, ulcers about the knees the ankles or the tendo Achillis were the most refractory. For ulcers more than 8 sq. cm. in size the average dose of tartar emetic required was 0.57 gm. and the time of hospitalization 28 days. Those treated as out patients responded less favourably in that they needed more injections and longer treatment. Since the mode of treatment was the same it is thought that the out patient removes the dressings to look at the ulcers or ascertain progress or applies village treatment also or gets the dressings soiled.

H. Harold Scott

DIVIZ O. Ainda o tratamento de úlceras pelo processo de Zeno (18 observações e breves comentários) [The Treatment of Ulcers by the Zeno Process.] *Brasil Medico* 1945 Apr 21 & 28 v 59 Nos. 16 & 17 129-36 29 figs.

The method of treatment here referred to is that recommended by Professor Zeno in 1943 for burns. Based on a dictum of Bohler that the best fluid for

regeneration of an infected wound is the wound's own secretion at the body temperature. Zeno went further and added that the tissues were damaged by the use of antiseptics and that the essential of cure was that it should not be hindered by any movement—in other words absolute rest and non-interference were the essentials. He therefore, treats chronic ulceration by plaster dressings after cleaning the surface and to mask the foul smell of these ulcers he first applies to them layers of gauze impregnated with 12 per cent. lactose. The plaster is left on [it would appear from these notes of cases] for 3-4 months after which it is removed and cure is nearly complete in most by this time. If not a second dressing is applied and removed after 4-6 weeks. Pain is relieved early. The author gives brief notes of fifteen patients with chronic ulcers—three of them had two ulcers and in one the ulcer had persisted for over 20 years.

Photographs are reproduced showing the conditions before and after treatment. Of the 18 ulcers so treated, eight were completely healed, five almost healed, four had improved and in one only was the lesion found to be worse and extending when the plaster was removed. This was a man of 22 years who had suffered from the ulcer for seven years. The plaster was applied in his case on January 18th 1944 and removed on March 9th. No reason is offered for the failure in this instance.

H. Harold Scott

WARD R. L. & MASON A. S. Polynuritis after Jungle Sores. A Series of Twenty-One Cases. *Brit Med. J.* 1945 Aug 25 252-4.

Many British and Indian soldiers developed multiple indolent ulcers known as "jungle sores" during the recent campaign in Burma and several British, but no Indian, soldiers afterwards suffered from peripheral neuritis. Among 21 patients in hospital with peripheral neuritis, 11 were admitted for neuritic symptoms, nine for malarial relapses and one for jungle sores—all had suffered from jungle sores the number of ulcers now healed, varying from 2 to 40 per man with an average of 14. The commonest sites were the lower leg and forearm. The sores had taken from 4 to 17 weeks to heal, the average time being eight weeks.

The typical jungle sore was a circular or oval punched-out ulcer about $\frac{3}{4}$ inch in diameter with a necrotic sloughing base and unhealthy purple edges.

In 16 cases the first symptom of nervous involvement was blurring of vision usually noticed after reading a few pages of print—it began from 4 to 12 weeks after the jungle sore appeared and lasted for about four weeks after which vision became normal. All the patients had sensory symptoms—tingling numbness and coldness of the extremities, and some also complained of difficulty in writing and walking. Astereognosis and ataxia also occurred.

Neurological examination showed the following conditions—Paresis of the lower neurone type greatest in the hands and feet, spreading peripherally but recovery took place in the reverse direction—the extensor muscles were more affected than the flexors. Its distribution did not correspond with that of the jungle sores. All forms of impaired sensation including postural sense occurred and corresponded to the paresis.

The muscles were not wasted and were rarely tender—tendon reflexes were absent in the affected limbs. Paralysis of accommodation was a marked feature of the disease, but in the few cases in which blurring of vision occurred in the hospital the pupils reacted to both light and accommodation. Apart from these signs the general bodily state of the patients was good. Details are given of three cases.

The authors discuss the differential diagnosis and conclude that the polynuritis was due to infection of the jungle sores with diphtheria bacilli—these

were isolated from the sores of the one patient in hospital who had unhealed sores and a week later he developed diphtheria of the throat. The origin of the diphtheritic infection in these cases remains obscure [The veldt sore of South Africa was found as long ago as 1901 similarly to be associated with the diphtheria bacillus]

J F Corson

WAR MEDICINE Chicago 1945 June v 7 No. 8 385-9 Cutaneous Diphtheria
War Department Technical Bulletin TB Med 143

MISCELLANEOUS DISEASES

BHATTACHARJYA B P Tropical Pyomyositis (Bung-Pagga's Disease) *Indian Med Gaz* 1945 Mar v 80 No 3 139-40

Three cases of tropical myositis [intramuscular abscess] in soldiers (race not stated) were treated at the Combined Military Hospital at Roorkee India. Sulphathiazole was given with little or no effect some of the abscesses were incised and others subsided spontaneously [Bungpagga was a tribal name for the disease in the Northern Territories of the Gold Coast see this *Bulletin* 1917 v 9 53]

J F Corson

FALCÃO P C. Contribuição ao estudo do rinoscleroma no Brasil. [Rhinoscleroma in Brazil] *Brasil-Médico* 1945 Apr 21 & 28 v 59 Nos. 16 & 17 136-44 9 figs. [31 refs]

Among 16 000 cases observed in 1940 by the author there was only one of rhinoscleroma a Brazilian white man of 23 years of age. In 1940 he applied for treatment complaining of the nose and throat. The symptoms had begun three years before with attacks of dysphonia at times associated with dyspnoea. Then he began to feel increasing obstruction in the nostrils and they finally became blocked.

Examination revealed polypoid formations sessile or with short pedicles in both nostrils and others below the larynx extending into the trachea some with removable crusts. There was no enlargement of the cervical glands. Microscopically fragments of tissue removed showed the characteristics of rhinoscleroma. Frisch's bacillus was seen and cultivated. The morphological and cultural characters of this organism named *B. rhinoscleromatis* by Frisch in 1882 are described.

The author states that cases of this disease are rare in Brazil which cannot therefore be regarded as an endemic focus. Only 26 cases have been recorded in the country since 1890 when Lutz reported the first recognized case. Of the total 16 only were autochthonous six were Europeans one an African in three the nationality is not stated. 11 were males 11 females in four the sex is not mentioned. 11 were whites 12 were coloured three not specified. The author does not think the paucity of cases is due to failure to diagnose them but to the actual rarity of the condition.

H Harold Scott

- i. LAHA P. N. Bengal Splenomegaly With an Illustrative Case Report. *J. Indian Med. Ass.* 1945 June v 14 No. 9 199-200
- ii. J. INDIAN MED. ASS. 1945 June v 14 No. 9 201-2. [10 refs.] Bengal Splenomegaly

i. The patient was a Muslim male 25 years of age giving a history of irregular fever for six months. On coming to hospital he was pale and emaciated with a temperature of 99°F pulse 82, respirations 28 per minute spleen felt 3 inches below the costal margin and hard liver enlarged to 1 inch below. Red corpuscles totalled 1,290,000 white 5,400 per cmm haemoglobin 5.5 gm. per cent. polymorphonuclears 74 lymphocytes 20 monocytes 6 per cent. no parasites seen. Fragility haemolysis begins in 0.42 per cent. saline and is complete in 0.3 per cent. platelets 180,000 per cmm bleeding time 4 minutes 50 seconds coagulation time 7 min. 50 secs. Van den Bergh indirect positive. Nothing abnormal seen in stools or urine Wassermann reaction negative nothing abnormal from spleen puncture.

The anaemia and general health improved with parenteral liver therapy r.b.c. 2,100,000 white 4,150 per cmm (polymorphonuclears 48 lymphocytes 48, monocytes and eosinophiles each 2 per cent.) haemoglobin 7 gm., but there was no change in the size of the spleen or liver.

Such was the clinical condition typical in nearly every respect of what has been previously reported as Bengal splenomegaly (see this *Bulletin* 1933 v 30 43 1940 v 17 232 1944 v 41 144). In SEN GUPTA'S cases (the last of these references) the anaemia was orthochromic and macrocytic whereas in the case here reported it was hyperchromic.

ii. In a leading article previous reports are debated and the aetiology discussed in an able manner but no conclusion is reached. Sen Gupta's suggestion that it is basically due to hypersensitiveness to malaria infection leading to intense hyperplasia of reticulo-endothelial tissue and splenic enlargement itself leads to the question: Why does not the spleen show histologically some specific sign of malarial infestation? The editorial states: It is not irrational to conclude that Banti's disease and Bengal splenomegaly are not possibly one and the same clinical entity. This is not very clear does the third negative enforce or contradict the first two? *H. Harold Scott.*

CHABERT M. Notes sur le cancer chez les indigènes du Sud-Cameroun. [Cancer among Natives of South Cameroons.] *Rev. Sci. Méd. Pharm. et Ch. de l'Afrique Française Libre* 1943 Oct v 2, No. 4 377-406 2 pls. [29 refs.]

This paper is divided into two main parts: in the first the author after quoting the records of others on the subject of malignant tumours in tropical countries gives notes on 20 patients with new growths seen during five years from August 1937 to October 1942. Among these six were melano-sarcoma, eight were other forms of sarcoma (one of the ovary in a child of 12 years), four were primary epithelioma of the liver, one a secondary epithelioma of liver and one an adenoma of the testicle. Eleven of the 20 were males and the average age of these was 35 years; among the nine females the average age was 38 years. Thirteen of the 20 have died, three are still living (three years after the first observations) four have been lost sight of. The preponderance if one can speak of preponderance among so small a total of cases of malignant melanomas among females is noteworthy: only one was in a man. All those with cancer of the liver were men.

The second part of the article deals in a general discussion on cutaneous malignant melanomas and on primary epithelioma of the liver and is made up

of quotations from the literature on these subjects with passing comments but does not contribute anything fresh
H Harold Scott

EVANS H M Toxio Properties of Sting-ray's Sting. [Correspondence]
Brit Med J 1945 Aug 4 165

[Stingarees or sting-rays are rare in the coastal waters of Britain but are fairly common abroad. *Trygon pastinaza* is met with in Japanese waters. *Aetobatis narinari* the Bishop's ray. *Trygon sephen* and others in the Indian ocean. The sting ray has a long flexible whip-like tail ending in a bony spine with sharp cutting teeth and a sharp point. When the ray attacks he strikes the tail round the victim's limb or body and forces the spine in causing a deep lacerated wound.]

The author describes the symptoms in a case occurring in India and reported to him. The fish caused a stab-incision on the right foot. There were signs of bruising but little or no haemorrhage. Local pain was severe at first with numbness of the limb. In 45 minutes respiration was painful and became increasingly so. In 1½ hours spasm of the abdominal muscles set in with restlessness, nausea, dizziness and tingling of the extremities. The pain became more and more severe, morphia was needed and had to be repeated. Vomiting ensued. The pain on breathing and the muscular spasms continued for three days. Constipation was troublesome. The wound ulcerated and did not heal for a fortnight.

The author gives also an account of the symptoms in a case of jellyfish sting. These were closely similar to those of the sting ray especially the abdominal spasm and the obstinate constipation. From this it is argued that the venoms of both are of the same nature [a point too important to take for granted and calling for further proof]. As Madame PRISALIX has shown there are two toxic principles in the jelly fish toxin—congestin and thalassin.

H Harold Scott

FLECKER H Injuries produced by Plants in Tropical Queensland. *Med J Australia*
1945 June 23 v 1 No 25 636-7

GENERAL PROTOZOOLOGY

ALLI J H Tannic Acid Fixative Method for Staining Protozoa. *Milit Surgeon* 1944 Oct v 95 No 4 317-19 [10 refs]

In this method the author fixes faecal smears on cover glasses in the following mixture for 5 to 7 minutes—tannic acid 4 gm. 70 per cent ethyl alcohol 90 cc. glacial acetic acid 5 cc. phenol crystals 1 gm. After fixation and washing in tap water mordanting is effected in 4 per cent ferric ammonium sulphate for 1 to 3 minutes. The films are well washed in tap water and are stained with ripened 0.5 per cent iron haematoxylin or a solution of haematin crystals for 3 to 5 minutes. After washing the films are differentiated in 1 per cent hydrochloric acid in 70 per cent alcohol till the blueness has not quite disappeared. The films are then washed well in tap water, taken through the alcohols, cleared and mounted in Canada balsam. It is stated that in films stained by the above method the protozoa are well fixed and stained and ready for examination within half an hour.

C M Wenyon

STABLER R. M. Ingestion Processes on *Iodamoeba* (Protozoa) *J Parasitology* 1945 Feb., v 31 No 1 79-80 8 figs on 1 pl.

In a study of *Iodamoeba butschlii* from two cases of human infection the author noted that a varying proportion of the amoebae (11.7 per cent. in one case and 27.0 per cent. in the other) were provided with one to four tube-like processes which appeared to be concerned with the ingestion of food. Some were quite large up to $1\frac{1}{2}\mu$ in length and 6μ in breadth, others were shorter and narrower. Many of them were twisted, while some for at least part of their length were tubular. Food particles such as bacteria were seen to be ingested at the open extremities. It seemed that after persisting for some time the tube-like structures were subject to withdrawal, during which their margins stained more intensely. Examination of *Iodamoeba kueneni* from the chimpanzee and the Guinea baboon showed that this species formed similar projections which are like those described by WENRICH [see this Bulletin 1945 v 42, 388 in *Entamoeba muris* *E. ranarum* *Dientamoeba fragilis* and *Histomonas meleagridis*. The paper is illustrated by eight figures showing the character of the processes. C. M. Wenyon

TOMLINSON W. J. Human Chronic Toxoplasmosis. *Amer J Clin Path* 1945 Apr v 15 123 [Summary taken from *J Amer Med Ass* 1945, July 28 v 128 No 13 975]

The literature reveals that 13 cases of toxoplasma infection have been diagnosed at necropsy and three clinical cases have been diagnosed by recovery of the parasites from cerebrospinal fluid. Wenman, in a study of immunity in experimental toxoplasmosis found that chronic toxoplasmosis in animals produced a different picture from the acute disease. Human chronic toxoplasmosis has not been demonstrated. While removing the necropsy material on sickle cell anemia Tomlinson found an instance of chronic toxoplasmosis in a British West Indian Negro girl aged 10 years 8 months who died of sickle cell anemia in the Canal Zone and who had no symptoms referable to toxoplasma infection. The case therefore represents the first reported case of chronic asymptomatic human toxoplasmosis. Toxoplasma parasites were found in pseudocysts throughout the brain and in aggregates within myocardial fibers. They were not accompanied by inflammatory changes or necrosis.

GENERAL ENTOMOLOGY

LEVER, R. J. A. W. Entomological Notes. *Agric J Fiji Suva*. 1944 v 15 No. 2, 45-50. [17 refs.] [Summary taken from *Rev Appl Entom Ser B* 1945 July v 33 Pt. 7 104]

Notes are given on the breeding places of various mosquitos that occur in Fiji. *Aedes scutellaris pseudoscutellaris* Theo., was found breeding in February 1944 in leaf axils of *Alpinia* and more recently in fallen, broken shells of the introduced calabash (*Crescentia cujate*). In one case there was no water in the shell, but only a mass of damp leaf-mould in which the larvae pupated. Also larvae of *A. scutellaris korreicensis* Edw., which is confined to the Fiji Islands, were found in a hole in a tree (*Barringtonia speciosa*) containing only damp leaf-mould. *Culex fatigans* Wied and *A. aegypti* L. breed in large

numbers in diluted fowl manure if this is left about in tins. Recent research by Army medical units has indicated that *A. scutellaris pseudoscutellaris* may be a vector of dengue in New Guinea and this seems to be the case in Fiji also since it was more abundant than *A. aegypti* from August to October in certain parts of Suva and early in December at the height of the epidemic at Nadi. In experiments in April and May 1944 on the suitability of different kinds of dung for *Musca domestica vicina* Macq. the percentages of the larvae that pupated were 38 in pig dung and 64 in cow dung. Horses in the Suva Peninsula where the work was done are too rare to be a serious source of flies in the town area.

GINSBURG J. M. Mosquito Oils, Larvicides, Repellents, Outdoor Sprays and their Application. *Bull. New Jersey Agric. Exper. Station No. 711* New Brunswick. 1944 Apr. 12 pp. 2 figs. [16 refs.]

The problem of mosquito control varies greatly with the habits and type of breeding place to be attacked. In all cases permanent measures are preferable but where they are unpracticable or impossible temporary measures must be used and if necessary personal prophylactic measures also taken. Petroleum oil distillates are the best chemical larvicides developed. The requirements of a good specimen are quick toxicity to larvae and pupae, good spreading on all kinds of waters, rapid penetration through debris and vegetation, a stable and long lasting film, inoffensive odour to man, absence of injurious effect on fish, waterfowl and plant life and low cost.

Oils of low boiling range kill by immediate toxic effect after inspiration into the tracheal tubes while high boiling fractions kill by suffocation after the tracheal system has been blocked. Experiments with different types of oil show that a good specimen should contain sufficient low boiling fractions (up to 600°F) to ensure a rapid kill, and sufficient high boiling fractions to leave a lasting film. A combination of this type can be obtained in New Jersey at a cost of from 5.5 to 8 cents a gallon, of which 10 per cent distils at 430–450°F, 50 per cent at 510–555°F and 90 per cent at 630°F or higher. It has a gravity (A.P.I.) of 27–33, a flash point of 130°F or higher and a viscosity of 35–40.

It has been found that application to the sides of a breeding place prolongs the toxic action, by continuous downward seepage. When difficulty is met with in forming a continuous film it may be overcome either by power spraying or by the addition of a spreader to the oil, either 0.5 per cent crude cresylic acid or 3 per cent of a tar oil containing 25 per cent cresylic acid. The quantity of oil required varies from 25 to 60 gallons per acre.

In places such as ornamental pools where oil is not suitable various other substances may be used. The best is said to be an emulsion of an oil solution of pyrethrum which in the dilute form finally applied contains 0.007 per cent pyrethrins. Though cheaper in larvicidal costs than oil the more frequent application needed increases the final cost when this larvicide is used. Soap, phenol and Paris green also have their applications but the latter is not much used for general mosquito control on account of its specificity for anopheline larvae. The author favours power sprayers for the application of larvicide wherever possible.

Protection against adult mosquitoes may be secured by the individual use of repellents such as dimethyl phthalate or large groups may be protected by applying the pyrethrum oil water emulsion to the ground in places where open air meetings are to be held followed by spraying it into the atmosphere in the form of a fog on the windward side both before and during the meeting.

G. Macdonald

GORDON W. M. & GERBERG, E. J. A Directional Mosquito Barrier Trap. *J. National Malaria Soc.* Tallahassee Fla. 1945 June v 4 No. 2, 123-5 1 fig.

DE MEILLON B. PARENT M. & BLACK, L. O'C. Descriptions of New Larvae and Pupae of Ethiopian Culicid. *Bull. Entom. Res.* 1945 July 38 Pt. 1 85-101 5 figs.

JUKOVA, V. V. [Employment of "K"-preparation for Sandfly Control.] *Med. Parasit. & Parasitic Dis.* Moscow 1944 v 13 No. 5 93 [In Russian.]

The author describes the results of tests with bisethylanethogen—xanthic disulphide known as K preparation which was used as a repellent against sandflies. It was shown that sandflies are effectively repelled for 7-9 days and prevented from entering rooms through the open windows after the walls, ceiling and doors of a room had been sprayed with 0.5-1 per cent water emulsion of the preparation with soap as the emulsifying agent, the consumption being 200-400 cc. of the fluid per 1 cub. metre. Further experiments revealed that the same effect can be produced by spraying a single sheet and hanging it on the wall near the bed. Protection for persons exposed to the bites of sandflies such as night-watchmen is afforded on the one hand by impregnating the underwear with a 1 per cent emulsion of the preparation and, on the other by smearing the unprotected parts of the body with a vaseline ointment containing 3-5 per cent of bisethylanethogen and renewing it every 2-3 days. C 4 Hoare

VARGAS L. Nota sobre ceratopogonidos y Culicoides. Notes on the Ceratopogonidae and Culicoides. *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico 1945 Mar v 6 No. 1 41-9 3 figs. 28 refs. English summary.

"The author presents a condensed revision of the supposed or already demonstrated rôle as vectors of diseases assigned to Ceratopogonidae. He also gives a preliminary list of the species of the western hemisphere recording 14 species for Mexico of which three are new for the country. He includes drawings of the wings of *Coptosus piliferus* and male terminalia of *Cockerellia var. tristatulus*.

HILL, M. A. & GORDON, R. M. An Outbreak of Dermatitis amongst Troops in North Wales caused by Rodent Mites. *Ann. Trop. Med. & Parasit.* 1945 May 31 v 39 No. 1 48-52 21 refs.

An outbreak of dermatitis consisting of some sixty cases occurred among American troops stationed in North Wales following the refilling of mattresses with new straw. The rash consisted of itching and elevated papules 3-10 mm. in diameter surrounded by varying degrees of urticarial reaction. The epidemic ceased immediately the palliasses were subjected to steam disinfection and the same result followed the substitution of straw from another locality. The straw used to stuff the palliasses when examined in the store of the affected unit was found to contain rodent mites belonging to the species *Harmogaster oudemani*, *Hypaspis fensholtii*, *Eulaelaps stabularis*, *Poecilochernis spinipes* and

Cheyletus eruditus. Only the first two were identified in the bedding and palliasses of the affected men *H. senilis* being present in large numbers. It is considered that some or all of these rodent mites were responsible for the dermatitis.
I B Wigglesworth

HURST H. Enzyme Activity as a Factor in Insect Physiology and Toxicology. *Nature* 1945 Aug 18 194-8 [13 refs.]

LABORATORY PROCEDURES

DAMMIN G J & WELLER T H. Heterophile Agglutinins and Cold Auto-haemagglutinins in Schistosomiasis Filariasis Malaria, and Leprosy. *Amer J Trop Med* 1945 Mar & 25 No 2 97-102 1 fig [19 refs]

At the Antilles Department Medical Laboratory, Porto Rico, the authors tested the Kahn positive blood sera of 273 soldiers for the presence of heterophile agglutinins and cold autohaemagglutinins. 199 were Porto Rican troops and 74 were United States soldiers stationed in Porto Rico. They had various infections. 104 sera were from patients with rectal schistosomiasis, 104 from cases of filariasis (*Wuchereria bancrofti*), 40 from cases of malaria, and 18 from lepers. The results are shown in tables and are summarized by the authors as follows —

In schistosomiasis 4.9 per cent had heterophile agglutinin titers over 1:32, in filariasis 13 per cent had titers above 1:32, and of the malaria cases 5 per cent had titers above 1:32. In no case was the titer higher than 1:128. In the small group of blood specimens from lepers, four showed a heterophile agglutinin titer of 1:128. Of twelve quinine-treated malaria cases, nine had a titer of 1:32 or lower and three a titer of 1:64.

Of the above group of 285 blood specimens, cold autohaemagglutinins in a titer of 1:10 or higher could not be demonstrated in 279 or 97 per cent. The few positive specimens showed no particular distribution and the highest titer noted was 1:80.
J F Corson

REPORTS SURVEYS AND MISCELLANEOUS PAPERS

MORRIS J N. Health of Four Hundred Millions. *Lancet* 1945 June 16 743-8 8 figs. [55 refs.]

In a fully documented article the author has painted a gloomy and depressing, but unhappily a true picture of conditions of life in India.

The infant mortality rate in 1912-15 was 204 per mille and although by 1938-42 the rate had fallen to over 160, it was more than three times as high as that of England and Wales for the same period. The death rate among Indian children between the ages of 1-5 years in 1938 was eight times as high as that of children in Britain. The expectation of life at birth in India was less than half the corresponding figure for England and other progressive western countries.

the concentration in the blood is measured again. The amount of dye which has disappeared from the blood is presumed to have been taken up by the reticulo-endothelial system. The ratio between the dye concentrations on the two occasions is called the Congo Red index and it is considered to be an indication of one aspect of the activity of the reticulo-endothelial system. In the present work 2 cc. of a 1 per cent. solution of the dye was injected intravenously and blood samples were taken after four and 60 minutes. Judged by this criterion, daily intramuscular injections of quinine (two monkeys) slightly increased the activity of the reticulo-endothelial system daily intravenous injections of diamidino stilbene (one monkey) diminished it and so did infection with *Plasmodium knowlesi*: the infection being partially controlled by quinine (three monkeys)

F. Hawking

BOOK REVIEWS

MAIR, L. P. *Welfare in the British Colonies*. 115 pp. 1944. London. Royal Institute of International Affairs. [3s.]

The essentials of a programme of colonial welfare are education, the control of labour and labouring conditions, the promotion of health, and a social welfare scheme which attends to other aspects of a community's well-being. The background on which they have developed, their history, their place in the administrative machinery of government and the present trends in their development are described in Dr Mair's book, one of several published by the Royal Institute of International Affairs with the object of encouraging and facilitating the scientific study of international affairs.

All of these subjects have developed greatly during the last twenty years, with accelerating speed as a result of a progressive Colonial Office policy. Education has developed from the efforts of scattered missionary schools to organized programmes, among ultimately, at universal instruction, but meantime trying to make as much headway as possible under difficult conditions, and showing a definite trend towards mass education, or the simultaneous training of persons of all ages in restricted localities in both literary, technical and domestic subjects and towards practical teaching of husbandry and domestic arts, though facilities for higher education up to University standards are steadily increasing.

The control of labour and working conditions is in most colonies a very recently accepted responsibility though Malaya started a Labour Department as long ago as 1911. In recent years the biggest problems have been encountered in connexion with mining and plantation industries in East and West Africa, as they attract large numbers of migrant labourers who need protection in making preliminary contracts, or in moving in search of work often over very long distances as well as when actually working. Considerable improvement has been achieved during a few years but standards are not always acceptable and continued effort is needed if good living conditions are to be assured.

The health of sixty million people of the Colonial Empire cannot be adequately cared for by the small numbers of doctors now available: the European doctors employed by the Colonial Government totalling only 700. In future the majority of the staff, both medically qualified and subordinate, must be of the

country in which they work and ample facilities for training must be available in every Colonial area. Medical education to a standard approved by the General Medical Council can be obtained in Ceylon Hong Kong Fiji East and West Africa and the Sudan but increased opportunities are urgently needed for the training of medical aids dressers dispensers nurses and technical assistants if medical attention is to be widely available. An outline is given of the measures taken to lessen the main tropical diseases and of the means by which simple treatment and sanitary instruction are taken to rural areas though it is clear that these are yet in their infancy.

The term social welfare covers an ill-defined group of services with the general object of co-ordinating public and private efforts to encourage desirable changes in social institutions and habits and alleviate distress. Most progress has been made in the West Indies as a result of the recommendations of the West India Royal Commission but a start has been made in other places a notable example being the Rural Welfare Service in Ceylon.

[This publication gives an eminently readable account of general trends of policy in welfare matters which would be of great help to the early student in becoming acquainted with the problems described for the first time. In the opinion of the reviewer it would succeed better in its object of facilitating the scientific study of colonial problems if it were more factual and gave fuller evidence of the gaps in the work done or critical comment on them.]

G Macdonald

BISPHAM William V [Colonel U.S. Army, ret'd] *Malaria Its Diagnosis, Treatment and Prophylaxis*, pp viii+197 frontispiece & 4 pls. (3 coloured) 1944 Baltimore The Williams & Wilkins Co London Baillière Tindall & Cox 7 & 8 Henrietta Street [£3 50 19s 6d]

This book was written to give the physician a knowledge of the clinical features of malaria. Its scope is not however limited to the clinical features of the disease. The chapter headings are History Geographic Distribution Etiology The Mosquito Epidemiology Symptomatology Complications Diagnosis Pathology Treatment Prevention Malarial Immunity Animal Experimentation Therapeutic Use Blackwater Fever Prognosis. A final chapter contributed by L. T. GOGGESHALL contains a brief description of the prevention and treatment of malaria in West Africa and is based largely on his experience while establishing the medical services for an air route from Bathurst Lagos Khartoum to Cairo.

Before publication various sections of the book were reviewed by one or other of twelve outstanding American malarialogists and their comments have been embodied in the text. This procedure should make the book authoritative but the result has not been altogether happy. Interpolations appear at times to be misplaced and there is a certain amount of unnecessary repetition.

The phraseology is sometimes loose and there are sentences that convey very little meaning. The chapter on symptomatology (p. 59) opens thus:

With most physicians the symptoms of malaria are confined to the paroxysm and periodic fever. This is a mistaken idea for the paroxysms are decidedly different for each type of fever and there are many other symptoms which should be considered. Further on in that chapter we read (p. 70) 'When the attack becomes pernicious the invasion of the peripheral blood becomes marked and the number of parasites observed gives an impression that most of the red corpuscles are invaded. This is not always the case and in some cases the amount of the invasion cannot be determined except by splenic puncture.'

On p. 132 occurs the statement 'In subtertian malaria coma is frequently a very dangerous symptom and it should be relieved as soon as possible

Intravenous injection of 3 cc. of a 40 per cent. solution of urotropin frequently clears up this condition promptly." This advice divorced from any other remarks about the treatment of cerebral malaria, might be disastrous.

Misprints are not absent. On p. 36 in describing Coggeshall's method of keeping parasites alive in infected blood, it is stated "The cabinet mentioned above is kept cold by solid dry CO_2 maintaining a temperature between 72 and 80°C.

The author's preference for intravenous as opposed to intramuscular injections of atabrine will not receive general approval (p. 124). Dr Coggeshall (p. 182) is of the opinion that atabrine should not be given intravenously this seems to be the accepted view.

Careful revision might make this a very useful manual. As it is, it is not a very trustworthy guide for the physician with limited knowledge and no practical experience of malaria. He might find it somewhat confusing.

Norman White.

TROPICAL DISEASES BULLETIN

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URINARY AMOEBIASIS

(A CRITICAL REVIEW)

By J M WATSON ARCS

Wellcome Laboratories of Tropical Medicine

Historical Survey

Urinary amoebiasis is rather a loose definition of amoebic infection in various parts of the urinary tract. The question of amoebic infection of the urinary tract has for long been vexed. At one time it was considered to be a relatively common condition especially in Egypt and South America. CASTELLANI and CHALMERS (1919) regarded amoebic pyelitis cystitis and urethritis as definite pathological and clinical conditions. Certain continental workers especially published a considerable number of records of alleged cases most of which however are now considered to be of dubious authenticity. Such authorities as CRAIG and FAUST (1943) STITT (1942) and MANSON BAHR (1940) in discussing amoebiasis dismiss amoebic invasion of the urinary tract as one of the rarest complications of the disease.

The earliest record of amoebae in the urine was made by BAEZ (1883) who found actively motile forms in enormous numbers in the urine of a young Japanese woman suffering from tuberculosis of the lungs and urogenital apparatus who died shortly after entering hospital. The urine which was removed by catheter contained pus blood and necrotic tissue. The amoebae which were about 50μ in diameter had granular cytoplasm and a vesicular nucleus and are stated to have been in every way similar to Lösch's *Amoeba coli*. Baez suggested that they represented a new species for which he tentatively proposed the name *Amoeba urogenitalis*, but there seems little reason to doubt that they were actually *Entamoeba histolytica*. Unfortunately no examination of the faeces was made so that the existence of a concomitant intestinal infection remains in doubt.

Subsequently JURGENS (1892) KARTULIS (1893) POSNER (1893) WIJNHOF (1893) and McDILL and MUSGRAVE (1905) claimed to have found amoebae in human urine but it seems probable from the somewhat inadequate accounts which they give that the bodies they observed were not Protozoa.

CRAIG in 1911 recorded an undoubtedly genuine case of urinary amoebiasis but in this instance there was a heavy intestinal infection and the amoebae were frequently discharged into the urine through a fistula which had formed

between an ulceration of the rectal wall and the wall of the bladder to which it was adherent. There was therefore no actual infection of the urinary tract in this case.

Cases of amoebic infection of the urinary tract have also been reported by JEFFRIES in 1904 (according to FANTHAM 1916) and by SIMONIX in 1914 (according to FIESSINGER and PARTURIER, 1926) but the reviewer has not been able to trace these papers.

A somewhat dubious case was recorded from Shanghai by FISCHER (1914) which, from the description may possibly have been authentic, but unfortunately insufficient details are given to enable a decision to be made. Also in 1914 LYNN reported amoebae, blood and pus in the urine of a patient who is stated to have used the same syringe for washing out both the rectum and the bladder but as no amoebae were found in the stools, this case is extremely doubtful.

In 1915 WALTON published an account of what seems to be one of the few undubitably genuine cases of urinary amoebiasis. Numerous actively motile amoebae were found in the urine of a male Indian suffering from haematuria and anasarca of the legs, penis and scrotum. The urine was scanty, blood stained and of "acid reaction" with a specific gravity of 1019. The patient, who was considered to be a case of chronic Bright's disease, gave no history of previous dysentery, but amoebae were found in the stools. A careful description is given of the amoebae from the urine from which it seems clear that the organisms in this case really were living specimens of *Entamoeba histolytica* although from the dimensions given they must have represented an unusually large strain. Injection of the urine into the rectum of kittens was however without result. Walton remarks that "probably an abnormal condition of the urine is necessary for the parasites to establish themselves."

MACFIE (1916) reported five cases of urinary amoebiasis from the Gold Coast, of which one only is adequately described from his account it seems possible that the organisms which he found in this instance were *Entamoeba histolytica*. Dubious cases were reported about this time by WARD, COLY and FRIEL (1916), FRIEL (1917), WRIGHT (1917) and CHALMERS and O'FARRELL (1917). According to FIESSINGER and PARTURIER (1926) KOSTER (1918) collected fourteen cases of urinary amoebiasis while BARTLETT (1917) found the condition to be common but the reviewer has not been able to consult the original paper. In all these instances the evidence for the occurrence and identity of the parasite in the urine is inadequate for a decision to be reached. It seems likely, as DOBELL (1919) has remarked, that diagnosis rested on errors of observation and interpretation.

In 1918 ARAVANTIXOS and MICHAELIDIS recorded the occurrence of active uninnucleate amoebae in the urine of a Greek boy suffering from cystitis. No figures or description of the alleged amoebae are given but the authors did not consider that they were *E. histolytica* and DOBELL (1919) has suggested that they were probably degenerating forms of *Trichomonas vaginalis*.

DOBELL (1919) in discussing the question of urinary amoebiasis came to the conclusion that there was no reason why *Entamoeba histolytica* should not occasionally occur in the urine but that such infection of the urinary tract must always be secondary to a primary infection of the large intestine. This author considered that of the cases recorded up to that date the only one which could be regarded as undoubtedly genuine was that of Walton.

Since the publication of Dobell's monograph a large number of cases, most of them of very doubtful authenticity, have been recorded. BAYMA and FAGUNDES (1918) published a brief note of a case of acute cystitis in which numerous active amoebae and cysts occurred both in the urine and in the stools but no details are given. NOGUEZ (1919) found what he believed to be

amoebae in the urine of a schistosomiasis patient who was suffering concurrently from amoebic dysentery. LEGER is stated to have identified these organisms as *E. histolytica* and the genuineness of this case is therefore hardly in doubt. There is a reasonable possibility that amoebae from rectal or intestinal lesions may have reached and passed through the bladder wall in the wake of the schistosome eggs. DE MELLO (1919) recorded a doubtful case. JACKSON in 1922 described an amoeba like organism found at autopsy in the uriniferous tubules of the kidneys from a 15-months child who had died in convulsions from broncho-pneumonia and parenchymatous nephritis. Active division of these organisms was apparently going on in the tissues but neither the figures nor the description suggest that they were actually amoebae.

In the next few years a spate of papers describing alleged cases of urinary amoebiasis issued from Alexandria. Foremost protagonists of the alleged disease were PETZETAKIS (1923 a & b 1924 1925 a b & c) PANAYOTATOU (1924 1926 a & b 1930) and RALLI and PANAYOTATOU (1923). No useful purpose would be served by considering each of these papers separately especially as some of them are repetitive. These authors describe cases of cystitis and nephritis which are stated to be of amoebic origin although in only a few of them was there any history of previous or concurrent amoebic dysentery. Living and dead entamoebae—in some cases showing active protrusion of pseudopodia and containing red blood corpuscles—and occasionally also cysts are stated to have occurred in the urine. In all these cases apparently a cure was effected by intravenous injection of emetine and this was considered to be a further reason for identifying the organisms in question as *E. histolytica*. Petzetakis in particular was fully aware of the possibility of mistaking large phagocytic cells for amoebae and in one of his publications (1925 b) in which he discusses at length the whole situation with regard to this infection, he refers to this point. On the other hand although in two cases described in the same publication he made permanent preparations of the supposed amoebae using Heidenhain's iron haematoxylin the results were evidently poor since he gives no figure of the stained specimens and states that he considers this method of identification as unsatisfactory identification of the amoebae in the living condition being preferable. WENION (1926) considered these cases to be genuine, but this seems doubtful in view of the fact that intrarectal injection of the urinary sediment (not urine of WATSON) into a cat failed to produce any amoebic infection. The other cases recorded by Petzetakis are less fully documented, but in some of them (1923 b) acute amoebic dysentery also occurred and in spite of the fact that no satisfactory figures are given it must be considered that these may have been genuine although the possibility of the urine having become contaminated from the faeces does not appear to have been excluded. In 1924 and again in 1925 Petzetakis described a new species *Entamoeba polymorpha* from the urine of two patients suffering from urethritis but the inadequate description and crude figures make it seem very doubtful whether in fact these organisms were Protozoa. In one case described by PETZETAKIS and PETRIDIS (1925) amoebae were alleged to occur in the urine of a patient infected with *Schistosoma haematobium* and as usual emetine treatment is claimed to have eliminated them from the bladder but as pointed out above in such a case the amoebae may have reached the bladder from rectal ulcerations through lesions caused by the schistosome eggs. PETZETAKIS and MYLONAS (1924) described the form of ulcerations in the bladder believed to have been produced by amoebae.

With regard to the cases reported by PANAYOTATOU (1924 1925 a & b) it would seem that some of them at least may have been genuine since centrifuged deposits from specimens of the urine containing the supposed amoebae

were injected intrarectally into kittens producing a fatal dysentery with typical lesions. Unfortunately however from the account given, at any rate in the earlier paper it is not certain that these experiments were carried out with due precautions and under fully controlled conditions, and they must therefore be regarded with a certain amount of doubt especially in view of the comments later put forward by KHOURI (1929) and FARMAKIDIS (1930) working in the same locality (see below).

In considering the instances of amoebae occurring in the urinary tract recorded by PETZETAKIS and PANAYOTATOU and their collaborators it should be borne in mind that they regarded amoebiasis not as a localized infection of the intestine but as a generalized infection, spreading throughout the body by the blood and lymphatic streams to which PETZETAKIS (1925) applied the name *amibhemie*. Of this malady they considered amoebic dysentery to be the most frequent and best known of the various local manifestations which could arise. However it is now a well-established fact that amoebiasis is primarily an infection of the bowel, from which it may spread in metastatic fashion especially to the liver and sometimes to other organs.

Another protagonist of the occurrence of urinary amoebiasis was FRANCHINI (1925 a & b 1926). In several if not all of the cases recorded by this worker there was a concurrent intestinal infection of actual amoebic dysentery and, as in all such cases the possibility exists that the amoebae may have gained access to the urinary tract by a fistula between the bladder and the ulcerated rectum. The possibility of contamination of the urine was said to be definitely excluded.

According to PETZETAKIS (1925-6) and GIROLAMI (1936) other records of cases of urinary amoebiasis were published in 1924 by PEYROT, CHEYSSIAL and ARLO but unfortunately it has not been possible to consult the original papers of these workers and they must therefore be passed over without comment. REISS (1924) recorded two cases of what he believed to be amoebic infection of the bladder and regarded the organisms in question for what seem to be totally insufficient reasons as a new species of *Entamoeba*. As in one of his cases there was a previous history of amoebic dysentery and as cystoscopy revealed ulceration of the bladder wall, this instance may well be genuine. Somewhat dubious cases of amoebic infection of the urinary tract were also recorded in 1924 by CARONARO and by WORSLEY and BATEMAN in both of which it was considered by the authors that the kidney was possibly infected, but the evidence is unsatisfactory. VICHREV (1925) recorded a case of infection of the vagina and bladder with *Amoeba urogenitalis* and other alleged cases of urinary amoebiasis were reported by BUCHMANOV (1925) from Palestine and by BALRAMELLI (1926) and VIVIANI (1926) from Italy.

EVANS (1926) in an important paper on the surgical aspects of amoebiasis throws doubt on the allegedly frequent occurrence of infection of the urinary tract with *E. histolytica* remarking that—apart from direct extension of the liver—amoebic abscess of the kidney has not been recorded. This author also states that he has never met with a genuine case of amoebiasis of the genito-urinary system and that he regards this part of the body as exceptionally resistant to amoebic infection.

Records of further cases of urinary amoebiasis continued to be published, particularly by workers in the Mediterranean region and in South America. CASTEX and GREENWAY (1926) reported the occurrence of amoebae in the urine from cases of nephritis. FIORITO (1926) recorded a possibly genuine case of amoebic cystitis in a female who had suffered from amoebic dysentery for three years and in whom deep intestinal ulceration had favoured the passage of the amoebae to the bladder by the lymphatic route. FIESSINGER and PARTURIER (1926) published a further detailed account of a possibly

genuine case together with a useful historical review. GOYENA (1926) also recorded what might have been an authentic case in which vegetative and cystic forms of *E. histolytica* occurred in the urine of a dysentery patient from this account there seems to be a distinct possibility of a fistula from the intestine to the bladder having permitted the passage of the amoebae but as usual the evidence is insufficient. A somewhat similar case was recorded by PAWAN (1928).

An especially valuable contribution to the problem of urinary amoebiasis was made in 1926 by CARVAILLO and SAUTET. These workers were led by the increasing number of reported cases of urinary amoebiasis to attempt to reproduce the disease experimentally. Using kittens which as is well known are peculiarly susceptible to infection with *E. histolytica* they sealed the urinary meatus with a collodion plug performed a median suprapubic cystotomy and inoculated cultures from a case of amoebic dysentery directly into the bladder. The collodion seal was removed after two hours. Although a number of such experiments were made none of the experimental animals developed any symptoms of urinary amoebiasis. At subsequent autopsy no bladder lesions were found (except one ulcer which did not contain amoebae) no amoebae were found in the urinary tract nor did any amoebae occur in the urine between inoculation and autopsy. From these results it is clear that *E. histolytica* does not readily establish itself in the bladder of cats.

YOKOCHI (1926) stated that amoeba could not live in urine. Unfortunately only an abstract of this paper was available and as the species of amoeba and the limit of concentration of the urine are not stated this evidence is very inconclusive. As the original paper appeared in a medical journal however it seems likely that the amoeba used was one of the human intestinal species.

SITSEN (1927) published an account of a case of amoebic abscess of the kidney discovered at autopsy. He discusses the numerous reports of amoebic infection of the urinary tract points out that many of these must be regarded as not satisfactorily proven on the evidence adduced and concludes that the amoebae may transfer from one site to another in the body via the lymphatic vessels.

A number of dubious cases of urinary amoebiasis were recorded by CHERE FEDDIN (1927) ROSSI (1927) VAN CUTSEM FRANCO (1928) ROCCA (1928) PIRANI (1928) SAUJEON (1928) and CHEVALIER and SOULIÉ (1928) in several of which there was no history of previous or concurrent dysentery. The last authors were alive to the possibility of mistaking haematophagous leucocytes for amoebae and realized that urinary amoebiasis was always a secondary condition, hence it is possible that some of their cases were genuine. However the principal evidence for the identification of *E. histolytica* in all these cases seems to have been ostensible cure of the condition by emetine injections. GUIDICEANDREA (1928) mentions an alleged case of combined bronchial and urinary amoebiasis showing abundant active amoebae in both urine and sputum.

In 1928 DESCHIENS and MELNOTTE reviewed the whole situation relative to amoebic infection of the urinary tract and cast grave doubts on the numerous reported cases of amoebic nephritis cystitis and urethritis. They pointed out that diagnosis on the grounds of either the occurrence of alleged amoebae in urine or the curative effect of emetine is completely inadequate that the identification of *E. histolytica* is not easy even for specialists various other cells and in particular large haematophagous leucocytes being readily confused with it unless differential staining with iron haematoxylin after wet fixation is carried out and that emetine when injected intravenously is beneficial in a variety of conditions especially haemorrhagic and congestive

conditions exercises a mild antiseptic and bactericidal action, and cannot be considered as exclusively amoebicidal. In Fez a notorious centre of amoebic infection, they examined the centrifuged deposits of 300 pathological urines but were unable to find any entamoebae.

KHOURI, in five papers (1924 1929 a & b 1930 1931) foreshadowed and later fully supported the comments of Deschiens and Melnotte and severely criticized the whole conception of urinary amoebiasis with special reference to the workers at Alexandria. In particular he pointed out the strong resemblance which large mononuclear phagocytes may bear to *E. histolytica* even down to the inclusion of red corpuscles—a point also remarked upon by ALEXEIEFF (1928 and 1927) and by THOMSON (1926)—and stressed that their identity could readily be proved by staining with iron haematoxylin or by cultivation in appropriate media. Commenting on the cases of urinary amoebiasis recorded up to that date he concluded that the condition is extremely rare but has been frequently diagnosed in error by clinicians in cases where no proof was brought forward of the occurrence of amoebae and that even where indisputable evidence of the occurrence of amoebae was produced, no scientific proof was put forward of the identity of the species or of its pathogenic rôle. Khouri not only examined 50 000 urine samples (over 1 per cent. of which contained blood) in not one of which was he able to detect any *E. histolytica* but he also made repeated examinations over a period of several years and invariably with negative results of the urine of a patient with haematuria, in which his colleagues claimed to have found *E. histolytica*. He asserts that without parasitological proof in the form of wet fixed iron-haematoxylin-stained smears showing the characteristic nuclear structure of the parasite and successful intrarectal inoculation into kittens, the allegation of the occurrence of amoebae in the urine must be regarded as erroneous.

FARMAKIDIS (1930) made similar criticism and emphasized that unremitting search over many years at Alexandria failed to reveal a single genuine case of urinary amoebiasis, despite frequent positive diagnoses by clinicians there.

Notwithstanding these criticisms records of alleged urinary amoebiasis continued to appear many of them without the parasitological proofs so justly insisted upon by the authors quoted above. Thus PENSO (1929 and 1932) GAMBER (1930) VENTURI (1930) SIGMA (1930) GERMANI (1931) BERNASCONI (1931) BRUNELLI (1931) STEFANO (1931) MATTEI (1932) and CROFFER and MITRA (1932) recorded dubious cases. Venturi in particular failed to produce any amoebic infection of a kitten by intrarectal injection of urinary sediment, and although he claimed to have made haematoxylin preparations which showed typical *E. histolytica* he reproduces only figures of fresh specimens which are singularly unconvincing. In Gamber's case there appears to have been a possibility that a fistula had formed between the bladder and an amoebic abscess of the rectal wall through which amoebae gained access to the urine. PANAYOTATOU (1930) re-affirmed her belief in the existence of urinary amoebiasis and its frequent occurrence at Alexandria in flat repudiation of the opinions of Khouri and Farmakidis.

PENSO in 1929 described a case of urinary amoebiasis which since no amoebae were found in the intestine he attributes to a new species *Entamoeba vesicalis* capable of producing a primary infection of the bladder. He does not, however state how such a species could gain entry to the urinary tract, and he records the remarkable facts that the amoebae remained alive in urine for a week, actually undergoing multiplication, and that they could not be stained by ordinary methods. Penso redescribed his amoeba in 1932. It seems certain, however, that he was dealing not with a protozoon but with degenerate cells. Nevertheless many authors subsequently attributed so-called primary cases of urinary amoebiasis to *E. vesicalis*.

DE MELLO (1931) reported one of the few undoubtedly genuine cases of the occurrence of *E. histolytica* in urine. The patient who was suffering from haematuria and strangury had no history of previous dysentery but was found to be a carrier. Wet fixed haematoxylin-stained smears showed typical active *E. histolytica* in the urine while some of the urinary deposit inoculated into the rectum of a cat produced a fulminating infection which terminated fatally.

DESCHENS in 1933 re-affirmed his previous comments and criticisms in relation to amoebic infection of the urinary tract. However some further unsatisfactory records of the condition were published by MOSCHINI (1932) GUIDICLANDREA (1932) CAPINCEFF (1934) GIROLAMI (1936) BACHRACH (1936) MANOHAR (1936) KOLLER (1937) and COUTTS and HERRERA (1942). In none of these cases were adequate proofs brought forward and they can only be regarded as unconvincing.

GIROLAMI's paper however includes an exhaustive historical review, a comprehensive bibliography and a critical discussion of the condition. He concludes that urinary amoebiasis is a definite clinical condition which is usually caused by *E. histolytica* and is then secondary to a primary bowel infection but which may sometimes be a primary infection due to *E. vesicalis* Penso. The figures of *E. vesicalis* which he gives are not convincing. HURD (1937) follows Girolami's conclusions.

Critical Discussion

From the preceding historical review it will be clear that in most of the reported cases of infection of the urinary tract with *E. histolytica* satisfactory evidence that the alleged organisms are amoebae is wanting and even granting that in some cases amoebae may have been present sufficient proof of their identity with *E. histolytica* is generally conspicuously lacking. In many of these cases too the possibility of the alleged amoebae being actually large haematophagous leucocytes or degenerating forms of *Trichomonas vaginalis* has not been definitely excluded. Certain types of leucocytes also bear a close resemblance to *Eutamoeba* cysts. Moreover no evidence is produced in those cases in which amoebae were actually present that they played a pathogenic rôle the symptoms attributed to their presence being such as are generally found in bacterial and other infections of the kidney, ureter, bladder or urethra in which inflammation has been set up. It will have been noted also that in most of these cases of alleged urinary amoebiasis the final diagnosis was based upon two inadequate premises, namely the appearance of amoebae in the urine examined fresh and the fact that the condition cleared up after treatment with emetine. As Deschens and Khouri have pointed out adequate parasitological proof of the presence of *E. histolytica* is rarely put forward while the fact that the condition cleared up under emetine therapy cannot be taken as evidence that *E. histolytica* was the causative organism since the effect of emetine is not confined to specific action upon this amoeba. Indeed KHOURI (1924) has shown that emetine treatment has a beneficial effect upon bilharzial cystitis, the symptoms of inflammation rapidly disappearing. With these considerations it must also be borne in mind that many of the workers cited above believed that amoebiasis was a generalized blood-borne infection of which amoebic dysentery was merely the most frequent manifestation. Though it is well known that amoebic infection of other parts of the body is always secondary to intestinal infection yet in many of the recorded cases of urinary amoebiasis no history of previous or concurrent dysentery was given by the patient and no amoebae could be found in the stools.

However the fact remains that certain cases notably those of BÄRLZ (1883) CRAIG (1911) WALTON (1915) MACFIE (1916) and DE MELLO (1931) were

undoubtedly genuine and upon the possible nature of these the recent work by WATSON (1945) throws some light. This author tested the ability of *E. histolytica* to live in media contaminated with various proportions of urine and was able to show conclusively that urine at 37°C is lethal to the parasite even when diluted to a quarter of its normal concentration. A few cursory tests along similar lines were made by MACFIE (1916) who stressed the harmful action of urine upon *E. histolytica* and noted the similarity of appearance between amoebae from infected faeces which had been immersed in urine and those from the urine of his patient. It is, therefore, doubtful if the parasite can ever exist in a medium of urine even as dilute as that in the kidney tubules. Watson however showed that some time must elapse before the effect of urine upon the amoebae becomes fully evident. Hence amoebae which gain entry to the lumen of the urethra or ureter or to the cavity of the bladder are doomed to extinction unless they can attack the wall of these organs where they will soon become protected from the urine by a crust of necrotic tissue and may multiply and produce characteristic lesions. Since they retain their active motility for upwards of two hours when immersed in undiluted urine quite a reasonable chance exists that some of the more vigorous individuals might penetrate the tissue of the urinary tract in this way. The process would obviously be facilitated, as MACFIE (1916) observed, by the prior existence of disease of some part of the urinary tract resulting either in altered composition of the urine (e.g. lower osmotic pressure, lower ammonia and urea content, higher pH) rendering it a more suitable medium for *E. histolytica* or in destruction of the protective epithelium lining the ducts and bladder and the consequent exposure of areas of the underlying tissue which might be more readily penetrated by the parasite. Presumably once amoebic lesions become established, active amoebae together with pus and necrotic tissue, would be extruded into the lumen by compression of the ulcer when the bladder contracts at micturition. The condition in which the amoebae would be found in samples of the urine would depend on how soon, after being passed the urine is examined. According to WATSON (1945) for a variable period up to about two hours the amoebae are able to retain their active motility but after a longer interval they become rounded and motionless and gradually degenerate as a result of the influence of the urine upon them.

With regard to the method by which the amoebae gain access to the urinary tract, there are four possible routes namely —

- (i) Direct access via the urogenital opening and the urethra.
- (ii) Entry from the gut into the bladder via a fistulous extension of an intestinal lesion.
- (iii) Entry into the kidney by extension of a liver abscess.
- (iv) Metastatic extension from the intestine via the blood or lymphatic channels.

There are thus four distinct conditions in which amoebae might conceivably appear in the urine in all of which it is evident that a primary infection of the intestine must exist and must serve as the original source of the organisms.

In respect of the first type urethral habits may lead to the transfer of active amoebae from the rectum and anus to the glans penis or labia and so to the urethral aperture where unless rapidly washed away in the course of micturition they might succeed in penetrating the tissues and setting up a urethritis or an ulcer of the glans itself as in the cases described by HERMANN and BERMAN (1942) and by SHIH WU and LIEU (1939). It is obvious that this type of case is liable to continual reinfection. Active amoebae may occur periodically in the urine at irregular intervals.

The second type may occur in individuals in whom the anterior wall of the rectum shows deep and extensive ulceration due to primary amoebiasis so that perforation of the rectal and bladder walls may occur in the region of the rectovesical connexions and active amoebae may gain direct access to the bladder. In such cases which are obviously only likely to occur in male subjects active amoebae will probably be found frequently in the urine having passed through into the bladder from the rectal wall. There may be some localized proliferation of the amoebae with consequent ulceration and necrosis of the wall of the bladder in the vicinity of the fistula. The establishment of the fistulous connexions between ulcerations of the gut wall and the bladder is less likely to occur at any other site owing to the freely movable nature of the bladder relative to the intestines at other points although it is of course possible that the development of adhesions elsewhere may facilitate the occurrence. A case of this type was described by CRAIG (1911) in which motile *Entamoeba histolytica* containing red blood corpuscles had been detected in the urine of a patient suffering from acute amoebic dysentery. A few days later the patient died and at autopsy a minute fistula connecting the bladder with an amoebic ulceration of the colon which was adherent over the bladder was discovered. Cases which may have been of this type were described by GOYENA (1926) PAWAN (1926) and GAMBIER (1930). A case of this kind is distinctly more likely to occur where amoebic dysentery exists concurrently with vesical schistosomiasis the bladder wall being already ulcerated by the passage of the helminth eggs. The case described by NOBLE (1922) may have been of this nature.

In respect of the third type it is well known that an amoebic abscess of the liver may ultimately, unless evacuated by operation become adherent to and discharge its contents into any of the adjacent organs. Rupture into the kidney in these cases although extremely rare may sometimes occur and an amoebic abscess of the kidney may then be formed. Inevitably amoebae will make their appearance in the urine sooner or later but are likely to be non motile and atypical from long exposure to urine. It is evident that infection by this route is more likely to lead to the establishment of the parasite in the urinary system with resulting ulceration and necrosis on account of the lower concentration of solutes in the urine of the kidney tubules than infection leading to the entry of the amoebae into the ureter bladder or urethra where the urine is more concentrated. CRAIG (1934) observed in San Francisco a case of amoebic abscess of the kidney due to perforation of an amoebic abscess of the liver into the kidney which was discovered at autopsy on a patient who had died of amoebic dysentery. Cases which were possibly of this nature were also described by CARONARO (1924) and WORSLEY and BATEMAN (1924) but in the absence of direct evidence from operation or autopsy it is unfortunately impossible to be sure.

Recently two cases of alleged amoebic perinephric abscess have been reported by KIRSH and DIAZ RIVERA (1943) and by ROSS (1944). No adequate evidence for the amoebic nature of these lesions however is put forward.

With regard to the fourth type it is known that extension of ulceration in the intestinal wall to include blood vessels permits active amoebae to enter the blood-stream and to be carried by the portal circulation to the liver and it is claimed that later when infection is established in this viscus, they may be carried to other organs such as the lung and the brain. In this way the parasite may reach and colonize the organs of the urinary system setting up characteristic ulcerations. The kidney is the organ most likely to be infected in this way and the same considerations will then apply as in the third type of urinary amoebiasis dead and atypical amoebae only being found in the

urine. It must, however be borne in mind that the possibility of infection of the urinary system in this way is extremely remote since the majority of the amoebae will tend to be filtered off in the pulmonary circulation or be carried to the brain before they have the chance of reaching the excretory organs.

CRAIG (1934) has laid stress on the large proportion (at least 60 per cent.) of fatal cases of acute or chronic amoebiasis, in which at post mortem some form of nephritis is found. He attributes this state of affairs to a peculiar susceptibility of the kidney to toxins which may be elaborated during the progress of the dysenteric infection and remarks that the importance of direct amoebic infection of the kidney in the production of such lesions is unknown. TRABAUD and MAIRE (1928) had previously reached somewhat similar conclusions as a result of observing nephritic symptoms in several cases of amoebic dysentery.

From the practical point of view the greatest difficulty in connexion with urinary amoebiasis is the question of diagnosis. The fact that the suspected condition clears up under emetine therapy is not proof positive of its amoebic nature. It must be emphasized that the typical active amoebae showing progressive motility and characteristic hyaline pseudopodia may very likely not be found in the urine unless it has been retained but a short time in the bladder and is examined immediately after it is passed. Non-motile and atypical forms of various types are more likely to occur especially if the urine is allowed to cool before examination, and these cannot be differentiated from large haematophagous leucocytes unless wet-fixed preparations are made and stained with haematoxylin, when the characteristic structure of the nucleus may be observed. Confirmation of the diagnosis might be obtained by cultivating the amoebae in a suitable medium by production of infection in kittens through intrarectal injection and by the complement fixation test. Moreover unless *E. histolytica* can be shown to occur in the intestine there is practically no possibility that it will be present in the urinary tract since cysts are only known to hatch in the gut.

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MALARIA

GARNHAM P C C. Malaria Epidemics at Exceptionally High Altitudes in Kenya. *Brit Med J* 1945 July 14 45-7

In June to August 1941 a severe epidemic of malaria occurred among a small farming community in Londiani (7 500-7 800 feet) 75 miles from the provincial centre Kisumu in Kenya. The Londiani district comprises a small township with an Indian bazaar and native location surrounded by European farms within a radius of about 12 miles. There was also a large military camp. Extensive areas of forest reserve border the farms in these live several thousand African squatters. The malaria epidemic chiefly affected the farms and the military camp there was but little malaria in the isolated huts of the African squatters. All but one of 27 positive blood slides showed *P falciparum* the one exception was *P vivax*. The epidemic ceased abruptly in August. Smaller outbreaks recurred in each of the three following years at the same season. Many cases were severe.

Seven species of *Anopheles* were found as larvae or adults or both: *A. gambiae*, *A. garnhami*, *A. natalensis*, *A. constanti*, *A. christyi*, *A. squamosus* and *A. kingi*. Of these species only *A. gambiae* is a known vector of malaria. Surveys showed that *A. gambiae* breeds for a short period at these heights about May and that adults persist for the next two months.

In 1944 there were 20 cases of malaria among 220 inhabitants of a farm 20 miles to the north of Londiani at an altitude of 8,300 to 8 500 feet here two adult *A. gambiae* were found in huts.

A mean temperature of not less than 61°F has been reported as the limit for *A. gambiae* breeding. This temperature is only attained in four months in Londiani February to May, the low rainfall of February precludes that month for *A. gambiae* breeding. The mean shade temperature is never sufficiently high in Londiani for the development of the sexual cycle of the parasite in the mosquito but *A. gambiae* spends most of its life in human habitations where the temperature is from 5 to 10°F higher than outside. The temperature in huts is just sufficient for the sporogony of *P falciparum* during the month of May about 66°F. The survival of *A. gambiae* through out the year in Londiani is extremely unlikely and it is reasonable to suppose that it is introduced annually by road or rail transport. *A. gambiae* can frequently be caught in railway coaches arriving in Kisumu.

Norman White

D ABRERA V St E. Malaria Parasite Findings in Blood Films in relation to Malaria Forecasts in Ceylon. *Indian Med Gaz* 1945 Feb. v 80 No 2 102-5 2 graphs.

In this study the author makes use of the relative frequency of the three species of malaria parasite found in blood films from patients attending two dispensaries at Wattegama and Katugastota in the basin of the Mahaweli Ganga alt. 1,500 feet throughout a period of twelve months. Similar observations made by SIVALINGAM from 1938 to 1941 at Ginulla in the basin of Maha

Ova, alt. 200 feet are also used [see this *Bulletin* 1943 v 40 746]. In these parts of Cevlon, where outbreaks of malaria are influenced by the vagaries of the monsoon *P. malariae* is most in evidence when the incidence of malaria is low. During seasonal or epidemic rises in malaria, *P. malariae* gives pride of place to *P. falciparum* and *P. vivax*. *P. falciparum* being chiefly responsible for epidemics. An attempt has been made to determine the point in the epidemic cycle at which *P. malariae* begins to give place to *P. falciparum* and thus to obtain due warning of the approach of an epidemic. The author has found $\log M/Q$ a useful expression where M signifies *P. falciparum* and Q *P. malariae* infections in any given month. The values so obtained are charted. When the curve attains the zero line it is a danger signal. In the three illustrations produced warnings of approaching outbreaks might have been available two months, two weeks and one month, respectively, before the event.

Norman White

DE OLIVEIRA CASTRO G. M. Ecologia do *Anopheles gambiae*. Pesquisas preliminares sobre a viabilidade dos ovos que ficam fora da água. [Ecology of *Anopheles gambiae*. Preliminary Study on the Viability of Ova away from Water.] *Mem Inst Oswaldo Cruz* 1943 June v 38 No 3 517-34. 1 graph. English summary (9 lines).

The author and others working apparently in 1939 before *Anopheles gambiae* was eradicated from Brazil, were surprised by the rapid and intense infestation of the Valley of Banabemu so soon after the early rains of the year. The valley just before had been apparently dry and free from *A. gambiae*. Ova for these experiments were obtained in the laboratory; they were passed on a piece of moistened filter paper on the top of a cushion of cotton wool saturated with water in a Petri dish. The laboratory was an emergency one in Aracati, Ceará State.

In the first series the ova were exposed to the ordinary atmosphere away from water. On the filter paper where they had been deposited, the drying thus taking place slowly within 36 hours. Seven days to a month later they were placed in water. None of the 1,655 ova left for seven days survived to produce larvae nor did any of 12,276 left for a month. GRUBB had previously reported that ova of *A. gambiae* would not, after four days away from water give rise to larvae.

Next the ova were kept away from water but in air saturated with moisture. They were placed, in lots of 50 or 100 on rectangular pieces of filter paper in small glass tubes with cotton wool (moistened and then squeezed out) at the bottom and the outlet was closed with a paraffined cork. Some which were to be kept at a low temperature were maintained at 14°C. As would be expected, a certain number of the eggs would become larvae and when the time for the test was reached these were counted and rejected, the remainder on the paper being placed in a Petri dish in the centre of which was a pad of cotton wool saturated with moisture but not enough to cause the ova to come into contact with the water. As controls other ova were maintained in water at the laboratory temperature. The results were as follows:—

1. Controls.—Of 537 ova remaining in the water from the time of oviposition at laboratory temperature 54 per cent. yielded living larvae 34.5 per cent. had dead larvae and 11.5 per cent. were sterile.

2. Of those kept at room temperature away from water five series of tests were made estimations being carried out at 8, 10, 15, 20 and 30 days:—

(i) 41.8 days.—Of 1,149 ova, 10 per cent. yielded living larvae 70 per cent. died in the tubes 14.4 per cent. within the ova and 5.6 per cent. were sterile.

- (ii) *At 10 days*—Of 1,250 ova 12.4 per cent gave living larvae 3 per cent were sterile and 84.6 had dead larvae (in the tubes or in the eggs)
- (iii) *At 15 days*—Of 1,564 kept for this period no living larvae resulted 2 per cent were sterile and 98 per cent had dead larvae
- (iv) and (v) —*At 20 and 30 days*—Readings of these were somewhat spoiled by growth of moulds on the filter paper. The ova were nevertheless transferred to water but no living larvae emerged.

3. *Kept away from water but at 14 C*

- (i) *At 15 days*—Of 1,325 ova there were 5 per cent with living larvae 4.2 per cent sterile and 90.8 per cent dead.
- (u) *At 20 days*—Of 924 there was 0.1 per cent living larvae 23.2 per cent sterile and 76.7 per cent dead.
- (in) *At 30 days*—Of 943 ova none yielded living larvae 9 per cent were sterile and 91 per cent dead

The effect of the sun's rays on pupation was noted. Larvae exposed to the sun pupated in a few hours even in a few minutes in some instances when kept in the laboratory away from the sun's rays they did not do so for days.

The conclusion is therefore that deprived of water the ova of *A. gambiae* do not survive for very long
H. Harold Scott

CORRÊA, R. R. & RAMOS, A. S. Notas sobre o estudo da biologia do *A. tarsimaculatus* em Caraguatatuba. [Notes on the Study of the Biology of *A. tarsimaculatus* in Caraguatatuba.] *Arquivos de Hig. e Saúde Pública* São Paulo 1944 v 9 No 20 103-8. English summary. [Summary taken from *Rev. Applied Entom.* Ser. B 1945 Aug v 33 Pt. 8 121.]

In view of the finding of malaria parasites in females of *Anopheles crucians* Komp (for which the authors use the name *tarsimaculatus* Goeldi) [see this *Bulletin* 1942 v 39 738] from houses in Caraguatatuba on the coast of São Paulo in 1943 a study of the bionomics of the larvae and adults of this Anopheline was begun. An account is here given of the methods used.

LEE, David J. & WOODHILL, A. R. The Anopheline Mosquitoes of the Australasian Region.

This book is reviewed on p. 1049.

ANDERSON, G. A., VON DESCHWANDEN, J., GRAY, W. A. & MENZIES, T. H. Die Malaria im Hochgebirgsklima. [Malaria in High-Altitude Climates.] *Acta Tropica* Basel 1945 v 2 No 2, 122-36.

This paper deals chiefly with the effects of the climate of Adelboden on patients suffering from malaria chiefly of the relapsing benign tertian type. Adelboden is a well known Swiss winter-sports resort situated at a height of about 4,300 feet. snow, frost and bright sunshine are the chief features of the climate in winter.

Most of the patients were British soldiers who had fought in North Africa and had escaped from Italian prison camps. they arrived in Adelboden in the months November 1943 to February 1944. There were 84 cases of benign tertian and four of malignant tertian infection. In 34 other cases of clinical malaria no parasites were found. Little information is given of the duration of the infection or of the previous treatment.

Although some of the patients received no specific treatment hardly any relapses occurred after March 1944 and the striking improvement in their general health was attributed to increased body resistance due to the bracing climate.

Their progress was estimated by systematic examinations of the blood by which remarkable improvement was demonstrated even in cases in which occasional parasitic relapses were still occurring. The blood changes indicating improvement were—A diminishing blood-sedimentation rate, an increase in the haemoglobin, red-cell count and colour index, a diminution in the number of the monocytes and in the degree of deviation to the left shown by the Schuller index. So long as these conditions remained abnormal treatment was regarded as necessary even if no parasites could be found.

John W. D. Megaw

CHAUDHURI R. N. & RAI CHAUDHURI M. N. Observations on Malaria and other Conditions seen in Burma Evacuees. *Indian Med Gaz* 1945 Feb. v 80 No. 2, 97-102.

During the exodus from Burma in the six middle months of 1942, 144 evacuees of many races were admitted into the hospital attached to the School of Tropical Medicine Calcutta. More than half of them had been on the road for six to eight weeks through most unhealthy country and were in poor shape. This paper is concerned with the diseases from which they suffered. One hundred and five were suffering from malaria, 62 per cent. of them *P. falciparum* infections. Four had typhoid fever complicated by malaria. [see also SCOTT this *Bulletin* 1920 v 15 252.] There were only two deaths among the 144. Case reports are given of interesting cases together with a mass of miscellaneous information.

Norman White

HYMAN A. S. Clinical Masquerades of Malaria. Observations in South Pacific Combat Areas. *U.S. Nav Med Bull* 1945 Aug. v 45 No. 2, 287-303.

During the first eight months of the Solomon Islands campaign casualties who passed through an advance naval base hospital included a number of cases of malaria diagnosed as such and an equal number of patients suffering from malaria but admitted with other primary diagnoses. A series of 100 such patients admitted with mistaken diagnoses is the basis of this report.

Thirty-four cases had been diagnosed as diseases of the chest, 21 cardiac and 13 pulmonary. The cardiac diseases included angina pectoris, coronary thrombosis, paroxysmal tachycardia, auricular fibrillation, extra systoles and heart block. In all these cases the underlying diagnosis was not arrived at till a chill occurred and malaria parasites were found in the blood. In most patients the cardiovascular symptoms yielded promptly to antimalarial treatment.

The pulmonary diseases diagnosed included atypical or virus pneumonia (8), pleurisy (4) and lung abscess (1). They all responded to antimalarial treatment.

Twenty-eight patients were admitted with symptoms pointing to abdominal disease, nine disease of the stomach, including gastric and duodenal ulcer, eight disease of the gall bladder or liver or both, six disease of the spleen and three appendicitis. Illustrative cases are described in detail. Here again the occurrence of a chill and the subsequent discovery of malaria parasites indicated the true nature of the disease.

Twenty-one missed cases of malaria were admitted with diagnoses of bone or joint diseases. In general the picture was one of acute arthritis.

Some disease of the head was the diagnosis in 12 patients in 7 disease of the brain 3 of the eyes 1 of the sinuses and 1 of the mastoid. Five of the brain cases were admitted with a diagnosis of possible meningitis. Meningococcus meningitis was occurring in minor epidemic form in the South Pacific area at that time this partly accounted for the difficulty of diagnosis in field conditions.

The 7 remaining patients in this series were admitted with diagnoses of kidney disease 4 thyroid disease 2 scrotal disease 1

Most of the mistaken diagnoses were made during the early days of the Solomons campaign before most of the medical officers had become acquainted with the bizarre manifestation of South Pacific malaria. In the latter part of the period under review an outbreak of dengue added to the difficulties of diagnosis

Norman White

✓ ARBUSE D I Neuropsychiatric Manifestations in Malaria. U.S. Nav. Med. Bull. 1945 Aug. v 45 No 2 304-9

This short paper covers a wider field than its title indicates. Reference is made to the many forms of disease manifestation which may result from the malarial infection of the central or peripheral nervous system. Here the author covers familiar ground. He writes with experience gained in the South Pacific area.

The psychiatric manifestations ascribed to malaria may be personality changes expressions of the patient's experience of the disease psychotic symptoms perhaps directly referable to the location of the cerebrovascular thromboses or a recognizable disease such as schizophrenia or manic depressive psychosis. In many cases transient attacks of depression were noted. In general the psychic symptoms were consistent with the mental make-up of the patients but they may have been activated by malaria. The rapid response and improvement in the mental symptoms with anti malarial therapy indicates a direct causal relationship in many cases. It is however reasonable to suppose that the secondary symptoms such as depressed and paranoid states depend to a considerable extent upon the mental make-up of the patient before he contracted malaria and that in such cases malaria plays no different rôle from that of other organic diseases which may be followed by psychoses.

Norman White

✓ HARVEY A. M. A Type of Neuritis associated with Malarial Fever. Bull. Johns Hopkins Hosp. 1944 Oct. v 75 No 4 225-31

The author reports that in an army general hospital a large group of patients suffering from malaria developed signs and symptoms of peripheral neuritis which are described. In the mild cases one or more of the extremities went to sleep easily and there were frequent attacks of numbness and tingling. In some cases there was hyperalgesia and hyperaesthesia over the distribution of a peripheral nerve or a posterior root. The symptoms usually increased in severity during subsequent attacks of malarial fever. More severe cases started with sharp pain in the involved region which was followed by sensations of cramp in the muscles. The flexor surfaces of the forearms and hands were usually involved. There was hyperalgesia and increased sweating. The flexion contraction of the muscles in the area could be passively reduced but this caused a great deal of tingling and pain.

These neuritic symptoms may develop during the latent phase of malaria while the patients are taking suppressive treatment. All the patients had mild recurrent attacks of malaria and all but one were infected with *P. vivax*. The exception had a *P. falciparum* infection.

Norman White.

KELLNER, A. HOCHSTEIN, E. & THILMAN, A. J. B. Spontaneous Rupture of the Spleen in Malaria. Fatal Case. *J Amer Med Ass* 1945 Aug 25 v 129 No 17 1227-9

RAVDIN, I. S. & NORTH, J. P. The Simultaneous Occurrence of Acute Appendicitis and Malaria. *Ann Surgery* 1945 Sept v 122, No 3 432-5

DAVIDSON, S. Experimental Investigation of Burasaine in the Treatment of Malaria. *East African Med. J* 1945 Mar v 22, No 3 80-85.

The author reports the treatment with burasaine of 15 non-immune and 3 immune Africans suffering from *P. falciparum* malaria. Burasaine comes from Madagascar. It is the total alcohol extract of the root of a tree *Burasia madagascariensis* Thouars (family Menispermaceae). The extract contains alkaloids with the methyl-orthoquinone-noquinoleic ring such as is found in hydrastine and berberine. The extract was made up into tablets of 5 grains each. Sixteen tablets were given each 24 hours. Swallowing the tablets with water often caused nausea and vomiting so each dose of four tablets was dissolved in two ounces of glucose water and 10 minims of dilute hydrochloric acid were given. No toxic effects except vomiting were noted. Three non-immune control cases were treated with quinine.

All but one of the patients treated with burasaine only left hospital free from fever and parasites in the peripheral blood. The resistant case was given quinine on the 19th day and recovered. Burasaine acts very much more slowly than quinine though from the data supplied it is not possible to make any exact comparison of the efficacy of the two drugs. It would seem that burasaine has some definite antimalarial properties. *Norman White*

PIRK, L. A. & ENGELBERG, R. Hypoprothrombinemic Action of Quinine Sulphate. *J Amer Med Ass* 1945 Aug 11 v 128 No 15 1093-5 2 charts

The authors have found that the administration of quinine sulphate to normal adults in daily doses as small as 0.3 gm. is accompanied by a significant rise of the prothrombin time indicating a prothrombin-lowering effect of quinine sulphate. In carrying out the estimations the Page method was used, in which Russell viper venom and calcium chloride are added to plasma obtained by centrifuging decalcified venous blood. The sharp end-point is characterized by the formation of fibrin particles clearly visible in the agitated test tube. If vitamin K be administered with the quinine the fall in the prothrombin level does not occur. The vitamin K compound used was 2-methyl-1,4-naphtho-hydroquinone-diphosphoric acid ester tetrasodium salt, Synkavite Roche. The dose was 10 mgm.

The lowering of the prothrombin level of soldiers taking suppressive quinine would expose them to the danger arising from prolonged bleeding should they be wounded. The concurrent administration of vitamin K is recommended.

Norman White

DREIBACH, R. H. & HANZLIK, P. J. Antagonists for the Circulatory Depression of Quinine Injected Intravenously and the Implied Cholinergic Action and Nature and Importance of the Vasodilatation, in the Depression. *J Pharm & Exper Therap* 1945 Mar v 83 No 3 167-84 3 figs. [16 refs]

This is a report of an extensive study to discover effective antagonists to the circulatory depression caused by the intravenous injection of quinine. The

experiments were carried out on anaesthetized rabbits and cats the technique is described. An adequate summary of the paper is not possible in a small space. Some of the important results obtained are thus summarized by the author —

Of the 32 agents tried three mixed with the quinine in doses of 10 mgm. per kgm were capable of preventing or mitigating the depression namely epinephrine 0.015 to 0.02 mgm. per kgm as the most efficient and desirable neosynephrine 0.05 mgm per kgm about equal to epinephrine and next in order and calcium chloride 10 mgm per kgm about equal to epinephrine 0.01 mgm. per kgm and least efficient and desirable Thianone hydrochloride 10 mgm per kgm also antagonized the depression but the reason for this was not apparent.

The following groups of agents were found not to be beneficial or desirable various colloids ephedrine and benzedrine calcium in high doses digitalis group certain vitamins a substrate xanthines reducing agents metabolic stimulants and a number of miscellaneous agents

The circulatory depression of quinine was found not to be a cholinergic phenomenon and atropine would be of no antidotal value in mitigating correcting or reversing the depressor action or in collapse from quinine injected intravenously

The peripheral vasodilatation of quinine intravenously was found to be an early phenomenon comparatively minor and evanescent and of little or no importance in the typical sustained depressor action of the alkaloid. The seat of the vasodilatation was in the peripheral blood vessels and not demonstrably central cardiac or cholinergic in origin

For a 70-kgm adult man the total doses of the most desirable agents for use in severe quinine collapse would be epinephrine 1.4 mgm or neosynephrine 3.5 mgm injected intravenously well diluted and cautiously Nikethamide 700 mgm might be permissible but would be more hazardous. However in severe collapse of quinine the cardiac poisoning may be and often is irreversible and therefore all treatments may be of no avail.

Norman White.

MACDONALD G. Need for Malaria Control Policy for Rural Africa East Africa & Rhodesia 1945 Aug 2 v 21 No 1089 1140-41

Macdonald reviews briefly the course of malaria in persons born and brought up in conditions of high endemicity such as exist in many parts of Africa. There is good *prima facie* evidence that it causes mortality in infants and morbidity at later ages on a large scale though the statistical evidence for the former is poor [The findings of the late E. C. SMITH in autopsies on children in Lagos are relevant. Death was attributed to malaria in 14.4 per cent of a series of 500. See this *Bulletin* 1943 v 40 496]. In spite of the fact that after a childhood of generally poor health attributable largely to malaria the adult arrives at a condition of relative immunity the author cannot agree with those who hold the view that this process should not be disturbed (other than by the administration from time to time of such small doses of curative drugs as may suffice to reduce fever) in case the people are deprived of the protection they ultimately achieve through the process of immunity. He quotes findings which indicate that a state of fever is common in childhood and even in adult life and argues that this morbid process is to the detriment of the people. Most workers would no doubt agree with this the argument of those who hold the view described above would be that at present there is no hope of so reducing malaria in rural Africa that the immune state would be unnecessary and that partial control would mean loss of immunity with more

severe reaction to infection, throughout life. Macdonald is not content with this view and points out that malaria can very largely be controlled in village communities by the spray killing of adult mosquitoes, and that this procedure is popular with the people. He advocates experiments on a large scale properly controlled, in which pyrethrum DDT and gammevane would be used for this purpose and be combined with control of larvae by hand-strewn paris green. He points out that most of the expense would be the labour and that any community can afford its own labour. Such experiments should be combined with research work and the whole project should be conceived on a big scale. At present there is no such large scale undertaking.

One possible effect of efficient malaria control would be an increase in the size of the populations. This would entail research on the whole subject of agricultural methods and other matters so that the land could support its people until a balance is achieved at a population considerably above that which now exists.

Charles Wilcocks

ANNECKE A. MCCARTHY D.D. & WILSON D. BAGSTER [Dr G. Macdonald's address on "A Policy of Malaria Control for Rural Africa."] [Correspondence *East African Med J* 1945 Sept. v 22 No 9 308-8.]

In this letter the writers join issue with MACDONALD (above) over his contention that malaria control should be undertaken on a large scale in the hyperendemic rural areas of Africa by the combined use of all the means at present available for such control. They argue that hitherto eradication has not proved possible in such areas and that success has been attained, by spray killing (the only economic procedure) only in places where transmission is seasonal. In places such as Freetown, where circumstances for control by all means are favourable and in which the population is partially treated and therefore not immune, control should be pushed to eradication, but over the wide hyperendemic areas, where full control measures are not practicable and where the result of attempts in the past has been merely to reduce the peak of malaria, the resulting diminution of immunity with prolongation of ill health throughout life would more than counterbalance any advantage gained. In such areas a partial control should not be attempted by present methods except on an experimental scale. The writers of the letter urge that such experiment should be vigorously undertaken, so that full advantage may be taken of opportunity for new developments. "What is needed is a new method and one which is much more efficient than any yet known—a single and cheap form of attack is required. To this end they suggest the creation of a Malaria Institute of Africa."

In the meantime and in view of the fact that malaria is only one of the many health problems of rural Africa, they suggest that creation of better standards of living and agriculture may lead to increased capacity to resist malaria without losing the essential mechanism of immunity and would counteract the ill-effects of the present state of under nutrition.

[A reader may ask how far in fact these two points of view actually diverge. The question seems to be limited to hyperendemic areas, since both would probably agree that control is desirable in places where transmission is not perennial, and where immunity is therefore not achieved. Annecke *et al* argue that in hyperendemic areas, control with present facilities cannot be successful but that bonification (in a wide sense) may increase resistance and retain immunity. Macdonald argues that control may lead to diminution of illness and that bonification may therefore be expected and should be encouraged. Both advocate trial and research, and both recommend agricultural reform. To the reviewer it seems that decision can be reached only through further

experiment in which each method is given trial under good and thorough conditions it seems unwise to argue too closely from spray killing work carried out before DDT was used. As both parties to this argument agree that malaria control should be attempted on an experimental scale in hyperendemic areas it remains to determine the size of the experiment *ceteris paribus* the bigger the experiment the more clear-cut the results. But it is time this controversy was decided]

Charles Wilcocks

RAIMA B L. Larvifield Fish of Kangra Valley—*Schistocephalus proglottatus* Indian Med Gar 1945 May v 80 No 5 273-5 1 fig [10 refs.]

BRUMPT E. Zooprophylaxie du paludisme. [Zooprophylaxis in Malaria] Ann Parasit Humains et Comparés 1944-1945 v 20 Nos. 3-4 191-208 [Bibliography]

SPECK J F & EVANS E A. Jr The Biochemistry of the Malaria Parasite II. Glycolysis in Cell-free Preparations of the Malaria Parasite J Biol Chem 1945 June v 159 No 1 71-81 [23 refs.] III. The Effects of Quinine and Atabrine on Glycolysis. Ibid 83-96 [32 refs.]

II It was shown by WENDEL [this Bulletin 1943 v 40 674] that lactic acid is formed from glucose by *P. knowlesi*. In the first paper of the present series SILVERMAN *et al* [this Bulletin 1945 v 42 448] showed that it is also formed by *P. gallinaceum*. In the present investigation the mechanism of its formation by *P. gallinaceum* has been studied by using cell free extracts of the parasite. Two different types of preparation were used the first was obtained by taking parasitized red cells with water and freeing the parasites from cell debris by centrifugation (haemolysate). It contained enzymes from red cells and parasites and was more active than similar preparations from normal red cells. The second preparation (extract) was obtained by extracting parasites which had been freed from red cells by the saponin method of CHRISTOPHERS & FULTON [this Bulletin 1940 v 37 190] or less satisfactorily by taking parasitized cells with water. The operations were carried out at 0°. The results indicated that these enzyme preparations from *P. gallinaceum* were able to phosphorylate glucose in the same manner as yeast extracts and could convert fructose-1,6-diphosphate to 3-phosphoglyceraldehyde and bring about the dismutation between the latter and pyruvic acid. [FULTON (this Bulletin 1940 v 37 509) found by manometric methods that *P. knowlesi* was unable to oxidize hexose di or mono-phosphate.] The cell free extracts of *P. gallinaceum* appear to convert glucose to lactic acid in a manner similar to that of other living cells.

III Quinine and atabrine were shown by SILVERMAN *et al* (see above) to inhibit glycolysis and oxygen uptake by *P. gallinaceum*. By investigating the effect of these drugs on the phosphorylation of glucose and the dehydrogenation of 3-phosphoglyceraldehyde and lactic acid by the enzyme preparations used above it was sought to throw light on their mode of action in malaria. Experiments of a similar nature were made at the same time with glycolytic enzymes from yeast and muscle. It was found that quinine in concentrations of from 0.0001 to 0.002 M inhibited the phosphorylation of glucose in haemolysates of normal chicken red cells but was much less active against similar preparations from parasitized cells. The inhibition corresponded to the amount of hexokinase—the enzyme which catalyses the phosphorylation—obtained from red cell material. In the case of atabrine at similar concentrations to those of quinine phosphorylation of glucose was inhibited in both haemolysates to the same extent. Each drug inhibited the action of yeast hexokinase but the

enzyme 3-phosphoglycerate dehydrogenase which is concerned in lactate formation, was not significantly inhibited. Lactic dehydrogenase in the cell-free preparations from *P. gallinaceum* as well as in ox-heart preparations was more effectively inhibited by atabrine than by quinine. The latter drug consistently inhibited glycolysis by muscle extract, and also phosphorylation of glycogen, as well as the reverse reaction of polysaccharide formation from phosphorylated glucose besides other enzyme reactions involved in sugar-phosphorus exchange. Considered in conjunction with the observations of SILVERMAN *et al.* on the inhibition of glycolysis by quinine and atabrine in the case of *P. gallinaceum* the present results suggest that these two drugs may interfere with the hexokinase and lactic dehydrogenase of the parasites. Similar results were obtained on the inhibition of glycolytic enzymes from other systems. The authors point out however that the drug concentrations employed by them are greater than those which obtain during therapy. It seems to them improbable that interference with the glycolytic mechanism of the parasites is of chief importance in the therapeutic action of these drugs but rather that their oxidative processes especially those concerned with lactic and pyruvic acid, are interfered with.

J. D. Fulton

PARADEIR W. L. O ciclo exoeritrocitário dos parasitos da malária. [The Exo-Erythrocytic Cycle of Malaria Parasites.] *Univ. Inst. Oswaldo Cruz* 1944 Dec. v. 41 No 3 489-83 3 pls 7 figs. [Numerous refs.]

BLACKWATER FEVER.

MARGRAITH B. G. HAVARD R. E. & PARSONS, D. S. Renal Syndrome of Wide Distribution Induced possibly by Renal Anoxia. *Lancet* 1945 Sept. 8, 293-6. [85 refs.]

The authors critically discuss the question of what is the direct or immediate cause of the pathological changes in the kidneys which are present in persons in whom, usually during an acute illness renal failure (with or without oliguria or anuria) occurs.

The onset of oliguria or anuria is commonly the first sign. In patients who survive there is also a postanuric period of impaired renal function with nitrogen retention and often a copious unconcentrated urine. This condition of the kidneys is distinguished from other forms of nephritis chiefly by the fact that the kidneys recover completely in surviving patients.

The macroscopical and microscopical appearance of the kidneys in fatal cases is described in detail and reference is made to various pathological states in which similar renal changes occur ("larval" or "necrotising" nephrosis, and prerenal azotaemia of FISHER) tubulo-vascular renal syndrome of MARGRAITH).

Anuria in many different diseases e.g. blackwater fever and cholera and in trauma in man and animals (in experiments) is discussed with reference to the views and suggestions of various authors. Three causes of the renal changes have been suggested: (1) Mechanical blockage of the kidney tubules. (2) the action of some injurious substance in the blood. (3) renal anoxia. The authors discuss these fully and conclude that the condition of the kidneys is probably caused by renal anoxia, usually secondary to peripheral vascular failure. [See also TOWN this Bulletin 1942, v. 39 163 459 in relation to cholera, and HILL *Bulletin of War Medicine* 1941 No 6 355 with regard to crush injuries.]

J. F. Corson

TRYPANOSOMIASIS

HUNT A R. & BLOSS J F E. Tsetse Fly Control and Sleeping Sickness in the Sudan. *Trans Roy Soc Trop Med & Hyg* 1945 Sept v 39 No 1 43-58 2 text figs 4 figs on 1 pl. & 1 graph. [13 refs.]

Sleeping sickness due to *Trypanosoma gambiense* has been endemic in parts of the southern Sudan for many years and has never been eliminated from the area round Temburu adjoining French Equatorial Africa. In this area there are many small rivers tributaries of the Yubu almost all of which are infested with *Glossina palpalis fuscipes*. *Glossina morsitans* also exists in the area but apparently is not connected with human infection it follows game and the inhabitants are persistent hunters whose activities tend to drive away the animals and with them *G. morsitans*.

Attempts have previously been made to control sleeping sickness in this region by the creation of special settlements along roads and by control of traffic with some but never complete success. As the disease was reduced however control measures were neglected many of the regulations were irksome to the people. The authors have not found *G. palpalis* more than 10 yards from water unless carried away by the host and in 1938 therefore they began the block method of control described by Symes and his collaborators [this *Bulletin* 1936 v 33 651 1937 v 34 542 1939 v 36 740].

The fly density in the Yubu area was small (average 9 to 12 per fly boy-day) compared with that reported by Symes from Kenya (168 per fly boy-day) and the blocks made by the authors were therefore considerably larger than those of Symes. barrier clearings were made 800 yards long and 400 yards wide. The maintenance of clearings was difficult but various cover crops were planted to replace the rapidly growing local spear grass of these the most successful was colopogonium. As the scheme progressed and the disease incidence fell the maintenance of small road river crossing clearings and of watering place clearings was discontinued, and the people were asked to maintain the barrier clearings as a civic duty this entailed less than one fifth of the work they previously did.

In the six blocks prepared in which fly boy paths were cut as close to the water as possible catching was done by teams of boys aged 11-16 the total staff now numbers six group leaders 26 section leaders and 220 fly boys who patrol 300 miles of paths.

The results are shown in a series of diagrams covering the past five years. These indicate very clearly the great reductions that have been made in the numbers of flies caught a catch as low as five or less per fly boy week had been attained over most of the area by 1943 and this rate has been maintained. Complete elimination of the fly is apparently not possible by these means.

In the Yubu area there were 65 cases of sleeping sickness in 1938 but only three in 1942 though in other areas outside the scope of this control the numbers had not diminished [these figures presumably refer to new infections diagnosed]. The disease therefore has very largely been controlled, in spite of the fact that many irksome restrictions have been removed.

Charles Wilcocks

BLOSS J F E. The Meridi Outbreak of Sleeping Sickness. *Trans Roy Soc Trop Med & Hyg* 1945 Sept v 39 No. 1 59-76 1 map 2 diagrams & 5 figs. on 1 pl.

In February 1941 an epidemic of sleeping sickness broke out near Meridi in Equatoria Province of the Sudan no indigenous case had previously been

reported from this area, though *Glossina palpalis* was fairly common along the Eadi river and *G. morsitans* in the more open country to the north. The trypanosome concerned was *T. gambiense*. The outbreak was very localized, and to control it the block method of Symes was introduced, a census made, and inspections of the population held every three months. By the end of 1941 a total of 47 cases had been found, in 1942 there were 25 new cases in 1943 there were none. Details are given of the construction of blocks and clearings, which were similar to those used during the Yubu outbreak (see HOLT and BLOSS above) except that at a later stage narrow (50 yards) rod clearings were substituted for the wider (150 yards) clearings at first made in two places. One feature was the use of bamboo and thatch screens one of which was erected at each end of a clearing. The screens were placed across the river and extended for 10 yards up each bank, and each was reinforced by two secondary screens further out from the river and overlapping the first. These were known as staggered screens. These screens acted as barriers against flies which might otherwise have entered or crossed the clearings since GIBBINS (this *Bulletin* 1942, v 39 442) has shown that such obstructions will deter the flies from travelling along the course of a stream. These were successful in improving the efficiency of barrier clearings.

The author remarks that on the subject of control of *G. palpalis* there are now two views: one favours the block method with continued fly catching and wide clearings between blocks, the other favours rod clearings relatively narrow but often of great length assisted by screens and controlled by periodic catches. Each probably has its place and further work is to be done to test the methods.

Diagnosis rested on the old method of gland palpation, by which up to 1,000 people can be tested in one day followed, in suspected cases, by gland puncture and blood examination after triple centrifugation. This is efficient to detect an outbreak provided that enough of the people are seen. The fly population of this area was low—never over 30 per fly boy week—and it seems that the flies do not migrate far from people and that they tend to infect those who use the same watering place. The disease can therefore establish itself when fly density is low and fly control must in consequence be thorough and effective: a safe low density would be under five flies per fly boy week with continuous catching.

The incubation period was long: cases were rarely found within six months of infection and it may be a year before the disease is recognizable. Germanin (or antrypol) and trypanamide were used in treatment but the author found that a course of six injections of germanin was insufficient for first stage cases and advises that all should be treated with the same full course (3 germanin followed by 5–10 trypanamide) as is given in second or third stage cases.

Charles Wilcocks

ERRATA

In the abstract of Dr A. F. FOWLER's paper in this *Bulletin* 1945 v 42, 541 the sentence "Trypanosomes were present in the cerebrospinal fluid in 33 of the 42 patients" should read, as explained by the author in his paper.

Positive C.S.F. means that there was either direct or indirect evidence of central nervous system involvement. Thus thirty-three cases i.e. 78 per cent., showed involvement of the central nervous system. The abstracter regrets to have overlooked this explanation of the + sign in the table.

In the title of the paper by EAGLE abstracted in this *Bulletin* 1945 v 42, 354 the Greek letter gamma was misprinted as V: the name of the drug should read γ -(p-Arrenosophenyl)-Butyric Acid.

HAWKING F The Absorption of 4 4-Diamidino Stilbene (Stilbamidine) by Trypanosomes and Its Blood Concentration in Animals. *J Pharm & Exper Therap* 1944 Sept. v 82, No 1 31-41 4 figs. [12 refs.]

It was shown by HAWKING [this *Bulletin* 1939 v 36 220] that trivalent arsenicals and acriflavine are rapidly absorbed by trypanosomes *in vitro*. The absorption of 4 4 diamidino stilbene (stilbamidine) by trypanosomes previously demonstrated by HAWKING and SMILES [this *Bulletin* 1942, v 39 238] with the aid of the fluorescent microscope has been further investigated as a guide to the mechanism of its trypanocidal action. Some determinations of the plasma levels of the drug were also made by the method of HERA and GRINDLEY [this *Bulletin* 1943 v 40 122] in mice and rabbits at various times after injection. It was found that living trypanosomes absorb a large amount of stilbamidine at 37 C but in contrast to the author's experience with acriflavine and trivalent arsenicals, dead trypanosomes do not absorb it in any appreciable amount. The value of the partition ratio of the drug (concentration in trypanosomes/concentration in surrounding fluid) diminished with increasing concentration of the drug over the range studied. The ratio was smaller than that for trivalent arsenicals or acriflavine indicating a less marked absorption of stilbamidine by the trypanosomes (*T. equiperdum* and *T. rhodesiense*). Stilbamidine is also absorbed more slowly than the other drugs and the amount taken up at 18°C. is negligible. The absorption process was shown to be reversible in the early stages. The quantitative estimation of the amount of stilbamidine in trypanosomes isolated from the blood of a treated animal provided evidence of its absorption *in vivo* by these parasites additional to that previously obtained by the fluorescent microscope. The drug disappeared rapidly from the plasma of treated animals. From the above results the amount required to kill a single trypanosome was estimated. In general the action of stilbamidine on trypanosomes closely resembled that of the other drugs mentioned, but the site of absorption on the parasite is probably different as judged by the facts of drug resistance [this *Bulletin* 1939 v 36 221] J D Fulton

KING H Chemical Structure of Arsenicals and Drug Resistance of Trypanosomes. Reprinted from *Trans Faraday Soc* No 265 1943 Dec v 39 Pt 12 383-7 [17 refs.]

The work of EHRLICH and others on drug resistance in trypanosomes is briefly reviewed. In regard to the mechanism of drug resistance YOREL MURGA TROYD and HAWKING [this *Bulletin* 1931 v 28 909] first showed by means of a biological method that normal trypanosomes removed reduced trypanamide from the medium whereas drug fast trypanosomes failed to do so. This fact was confirmed by HAWKING (*J Pharm & Exper Therap* 1937 v 59 123) by chemical means. Arsenophenylglycine and phenylarsenoxide were however absorbed by normal and resistant trypanosomes. GOUGH and KING (*J Chem Soc.* 1930 669) observed that a series of aromatic arsenic acids in which certain acidic groups were present were non-curative in experimental trypanosomiasis whereas the corresponding amides had curative properties. Later it was found that a number of arsenicals containing carboxyl groups in which the -As - linkage was present also possessed trypanocidal properties. Phenylarsen oxide as Hawking had found as well as derivatives with or without carboxyl groups proved lethal to normal and arsenic resistant strains of trypanosomes *in vitro*. From these facts it was concluded that arsenicals act primarily on trypanosomes in at least three different ways. The substances containing carboxyl groups form readily soluble highly ionized, neutral sodium salts and the ions do not readily leave the water phase a fact which may explain their

low trypanocidal power. One of the substances studied was 4-phenyl glycine arsenoxide and it is suggested that the anomalous behaviour of the phenyl glycine derivatives is due to the presence of the carboxyl group.

Non-ionized substances probably act on trypanosomes in a different way. Some arsenoxides without marked polar or hydrophilic groups are very active against normal and resistant trypanosomes *in vitro*. Since certain trypanosomes are known to contain large amounts of lipid material the author suggests that the active arsenoxides orient themselves at a lipid water interface so that the phenyl or corresponding group is in the lipid and the arsenoxide group is at the water phase whereby they are easily mobilized at the site of action on the trypanosome. Judging by the activity of certain members against both normal and resistant strains they act in a different way from the other substances studied. These latter types by which drug fastness can be produced, are possibly adsorbed on polar surfaces. The action of phenyl *pp*-diarsenoxide on normal and resistant trypanosomes was found to be similar to that of atoxyl, and the author therefore concludes that both ends of such molecules are involved in the primary fixation on the trypanosome. The final reaction by which the trypanosome is killed probably involves the arsenoxide group and the SH group in the living cell.

J. D. Fulton

ROMAÑA C. & MEYER, H. Estudo do ciclo evolutivo do *Schizotrypanum* Cruz em cultura de tecidos do embrião de galinha. [Study of the Developmental Cycle of *T. cruzi* in Fowl Embryo Tissue Culture.] *Mem. Inst. Oswaldo Cruz* 1942, v 37 No 1 19-27 12 figs on 6 pls. English summary.

"Chick embryo tissue cultures were smeared with *Schizotrypanum* from different sources. The cultures were inoculated with flagellates from blood-agar cultures and in one instance from blood of an infected guinea-pig.

Carrel's technique of tissue culture with slight modifications was employed.

The tissues used were spleen, myocardium, liver, epithelium of the iris, spinal ganglion and monocytes from chicken blood.

In all these tissues the flagellate developed easily parasitizing different types of cells: fibroblasts, histiocytes, macrophages, epithelial cells, cells of the nervous system, etc.

The authors were able to follow the complete cycle of the parasite, observing its classic evolution: transformation into leishmania, multiplication by binary division, transformation into tritrichia and finally into trypanosome.

They also observed forms of the parasite which possibly developed directly from leishmania to trypanosome without apparently going through the tritrichia stage.

They succeeded in infecting a white mouse with a human strain of *S. cruzi* after passage through tissue culture.

"The authors also pointed out different phenomena observed in the relations between the cells and the parasite."

VERY GUIMARÃES F. & JANSEN G. Novo transmissor silvestre do *Trypanosoma* (*Schizotrypanum*) *cruzi* (Chagas 1909). [A New (Natural) Transmitter of *Trypanosoma cruzi*.] *Mem. Inst. Oswaldo Cruz* 1943 June v 38, No. 3 437-41 3 text figs. & 3 figs on 1 pl. English summary.

In October 1942 the authors were carrying out research on American trypanosomiasis in the Santa Teresa district and found the opossum, *Didelphis*

aurea infected in nature and the transmitting insect *Panstrongylus megistus* similarly infected. In the course of their researches the authors found another bug only one-third to one-fourth the dimensions of the *P. megistus* naturally infected in the nests of the opossum in the branches or stems of the palm *Attalea indaya*. Sixteen specimens of nymphs and adults of this insect were examined and seven were found infected with the trypanosome. Infection was proved by inoculation of the rectal contents intraperitoneally into guinea pigs and the subsequent infection of the latter by xenodiagnostic methods 25 days later. The new transmitter is said to be closely allied to the genera *Belminus* and *Bolbodera*.
H. Harold Scott

LENT H. Novo transmissor da doença de Chagas na cidade do Rio de Janeiro. D.F. Estudo dos gêneros *Belminus* Stål 1859 *Bolbodera* Valdés 1910 e descrição de *Parabelminus carioca* n.g. n.sp. (Hemiptera Triatomidae). [A New Transmitter of Chagas's Disease in the Town of Rio de Janeiro, *Parabelminus carioca*]. Mem Inst Oswaldo Cruz 1943 June v 38 No 3 497-516 10 figs. [32 refs.]

The author has made a careful examination of the new transmitter of *T. cruzi* discovered by GUIMARÃES and JANSEN when carrying out investigations in the Santa Teresa district (see above). In the report of the latter it was stated that the insect appeared to be related to the genus *Belminus* or to *Bolbodera*. In the present article the author gives an account of the characters of each of these genera and shows that the new insect belongs to neither but to a new genus which he calls *Parabelminus*; he names the type species *carioca*. The affinities between the three genera are shown in a table and a very detailed account of the new vector is given in the letterpress with drawings of the various parts. The original should be consulted by entomologists and others interested as the details are too minute to be transcribed here (they occupy four pages of small print). [See previous paper for comparison in size between it and *Panstrongylus megistus*].
H. Harold Scott

LENT H. & DE OLIVEIRA S. J. Nota preliminar sobre a ação do DDT (dicloro-difenil-tricloroetana) em insetos transmissores da doença de Chagas. [Preliminary Note on the Action of DDT on the Insect Vectors of Chagas's Disease.] Rev Brasileira Biol 1944 v 4 No 3 329-31. [Summary taken from Rev Applied Entom Ser B 1945 Aug v 33 Pt. 8 132.]

An account is given of preliminary laboratory experiments carried out in Brazil with a view to using DDT [2,2-bis (parachlorophenyl)-1,1,1-trichloroethane] for the control of Triatomid bugs. In the first test *Rhodnius prolixus* Stål, *Panstrongylus megistus* Burm, *Triatoma sordida* Stål and *T. infestans* Klug were placed on petri dishes dusted with Neocade (5 per cent DDT adsorbed on talc). The action of the DDT was slow particularly on the immature stages, the later nymphal instars being the most resistant. One fifth instar nymph of *T. sordida* moulted after 10 days exposure to DDT giving rise to an adult that became paralyzed. Most of the bugs began to show signs of being affected after exposure for 18-24 hours but survived lying on their backs for several days. Pure, crystalline DDT did not appear to act more quickly than Neocade. DDT did not impede embryonic development; eggs of *R. prolixus* hatched after being left in a treated dish for 20 days.

In a second series of experiments 0.07-0.5 gm. pure DDT in gelatinous capsules was administered to pigeons weighing about 350 gm. on which individuals of *R. prolapsus* were later allowed to engorge. The results were somewhat contradictory. With doses of 0.07 0.2, 0.3-0.4 and 0.45-0.5 gm. the pigeons' blood was toxic to the bugs 3-6 12-20 1½-2½ and 1½-27 hours, respectively after the birds had ingested the DDT. The pigeons were not affected by doses of 0.4 gm. or less, but those that received 0.45-0.5 gm. were affected seriously and sometimes fatally and bugs that fed on them 1½-6 hours after they had ingested the DDT were affected within 1½-3 hours.

ROMAÑA, Cecilio & DIAS E. Reação de fixação do complemento na doença de Chagas com antígeno alcoolico de cultura do *Schizotrypanum cruzi* [Complement Fixation in Chagas's Disease, with Cultures of *T. cruzi* as Antigen. *Mem. Inst. Oswaldo Cruz.* 1942, v 37 No 1 1-10 [13 refs].

For preparing their antigen the authors grow the trypanosome in a medium of glucose broth and rabbit blood, haemolysed by distilled water. The details are as follows —

In a Roux flask is placed 100 cc. of nutrient agar after this is sterilized and cooled to 50-55 C. 10 per cent of rabbit (or sheep) blood is added and after being shaken is left to solidify. The surface is then covered with 100 cc. of glucose nutrient broth, pH 7.2. The medium is then seeded with 10 cc. of the trypanosome containing material (from man, opossum or bat) and kept at 20-25 C. for 15 to 20 days.

The fluid portion of the culture is then drawn off, the deposit is centrifuged and washed three times with saline. The fluid is again drained off and to the deposit is added ten times its volume of acetone and the mixture shaken repeatedly during the next 24 hours. After centrifugation, the deposit is placed in the incubator at 37 C. to dry and the product weighed. To this absolute alcohol is added in the proportion of 1 cc. to each centigramme of the powder. This is kept in a well-stoppered bottle for 20 days at 37° being frequently shaken. It is then fit for use.

Of 27 cases of Chagas's disease the sera of 26 gave a positive result, one was negative although xenodiagnosis was positive. Of 12 chronic cases with myocardial signs, guttre and mal de orelho (see this *Bulletin* 1921 v 18 301 1927 v 24 830 seven were positive. Of nine cases of cutaneous leishmaniasis seven were positive and the causative organism of this is closely allied to *T. cruzi* but in cases of syphilis, malaria, ankylostomiasis and other diseases, and 14 normal sera, all failed to give a positive reaction. One patient with yaws gave a positive but in this case there was a strong suspicion that he was suffering also from Chagas's disease.

H. Harold Scott

ROMAÑA, C. Contribuição ao conhecimento da patogenia da Tripanosomose Americana (Período inicial da infecção) [Pathogeny of the Initial Period of Infection in Chagas's Disease.] *Mem. Inst. Oswaldo Cruz* 1943 Dec. v 39 No 3 233-64 18 figs.

For studying the histology of the early stage of infection by *T. cruzi* the author scraped the inner aspect of the thighs of white rats and deposited thereon some drops of the metacyclic cultural forms of the trypanosome. Animals were killed and examined at varying intervals afterwards. One killed on the fifth day showed leishmaniasis and intracellular trypanosomes in the corium, subcutaneous cellular tissue and the subjacent muscle, but no cellular infiltration around the parasitized cells. There was a sparse infiltration with polymorphonuclears, eosinophiles, monocytes, some lymphocytes and histiocytes about the broken nests of parasites, and leishmaniasis could be

seen in the phagocytes. The one killed on the 7th day showed greater numbers of parasitized cells—there were no reactionary phenomena round the whole cells but infiltrative foci were more abundant and migratory histiocytes were numerous some enclosing the protozoa. On the 11th day the phenomena described were more marked—the cellular infiltration of the corium the subcutaneous tissue and the subjacent muscle. The inflammation was specially marked in the fatty tissue where many of the cells were parasitized. In the infiltrated area polymorphonuclears monocytes and histiocytes containing whole or partly destroyed leishmania were visible. The muscles showed similar changes their fibres showing parasites with no surrounding reaction except that those destroyed or broken were invaded by migrating phagocytes. There was also interstitial oedema of the corium and subcutaneous cellular tissue. The inflammatory phenomena were ascribable to the trauma of the raspatory not to the parasites. In brief, during the first period that of intracellular multiplication of the parasites infiltrative cellular phenomena do not occur these are not seen till 4 or 5 days afterwards in consequence of rupture of the parasitized cells.

Without scarification that is mere contact does not bring about infection or very rarely. The nasal mucosa is a site easy to infect the buccal mucosa less so.
H Harold Scott

COUCEIRO A. Lesões do ciático na infecção experimental de cães pelo *Schrotrypanum cruzi* (Nota prévia) [Lesions of the Sciatic Nerve in Experimental Infection of Dogs with *T. cruzi*] *Mem Inst Oswaldo Cruz* 1943 Dec. v 39 No 3 435-9 12 figs English summary (4 lines)

VILLELA and TORRES have described a paralysis occurring as a result of the experimental infection of dogs with *T. cruzi* but apparently no minute examination was made of the peripheral nerves and the present author believes that these played a part in causing the symptoms. VILLELA and TORRES ascribed the symptoms to central lesions and described them [see this *Bulletin* 1929 v 23 63 1927 v 24 593]. The author apologises for the small number of his observations the findings in four dogs (six were the subjects of experiment but two died of intercurrent disease) but what he has to record is quite definite.

Macroscopically the sciatic nerves showed no obvious inflammation or signs of degeneration but microscopically there was visible a perivascular infiltration of the vessels in the nerve-sheaths, with proliferation of the endothelium and perithelium and in both these leishmania were seen so that some of the capillaries seemed to be obliterated by them in others the leishmania decreased from the loose connective tissue cells to those of the neural sheath. In the cells of the perineurium they were distributed longitudinally or in rounded masses the myelin sheaths appeared in some places to be swollen and to stain poorly whereas others were normal. Though there is not evidence enough to show that *T. cruzi* has any true neurotropism the histological picture as regards the nerves is that of a neuritis predominantly interstitial.
H Harold Scott

MUNIZ J & DE FREITAS G. Contribuição para o diagnóstico da doença de Chagas pelas reações de imunidade. I. Estudo comparativo entre as reações de aglutinação e de fixação do complemento [Immunity Reactions in the Diagnosis of Chagas's Disease I. Comparison between Agglutination and Fixation of Complement.] *Mem Inst Oswaldo Cruz* 1944 Oct. v 41 No 2 303-33 1 fig [16 refs.] English summary

The primary difficulty in carrying out this research was to find a satisfactory antigen for the complement fixation test. Those of historical interest

were all tested from that of GUERREIRO and MACHADO in 1913 to that of DAVIS in 1943 [see this *Bulletin* 1943 v 40 890]. The pros and cons of each are given, but suffice it that the most recent one that of Davis proved the best, since it was a potent antigen, kept well, and was not anticomplementary to any appreciable degree. The details for its preparation are given [and are recorded in this *Bulletin loc cit*]. The sera tested numbered 54 altogether of these 6 were from acute cases of Chagas's disease 16 from chronic cases 7 from suspected. All these 29 were human patients in addition there were 4 animal sera, one of a dog infected with *T. cruzi* 2 of armadillos suspected of this infection, and one of a horse with *T. equinum*. There were also sera from 11 persons suffering from other diseases: malaria (3) yaws (3) leprosy (4) cutaneous leishmaniasis (1) and from ten normal subjects.

Twenty-four of the Chagas's disease patients were diagnosed by the finding of parasites in their blood or by xenodiagnostic methods, and all except one gave a positive complement fixation reaction. Thus one was positive to xenodiagnosis three others were positive to the complement fixation test but negative with xenodiagnosis. The leprosy malaria and yaws patients gave negative tests the one with cutaneous leishmaniasis was very weakly positive.

As regards the agglutination test all but one of the Chagas's disease patients gave a positive in a serum dilution of 1/160 to 1/10,240 the acute cases reacting in higher dilution (from 1/2,560 upwards) than the chronic (from 1/160 to 1/2,560). Those suffering from other diseases malaria and cutaneous leishmaniasis were negative but some normal sera and others from leprosy and yaws cases and the horse with *T. equinum* agglutinated in low dilution, none higher than 1/80. The two reactions, agglutination and complement fixation did not run *pari passu* one might agglutinate strongly but fix complement only in high concentration. The authors conclude —

Until further data on these reactions will be available complement fixation test is the most secure method for the diagnosis of this disease and the authors believe that with the introduction of Davis antigen and of methods for mass culture of the flagellates in accordance with the technic herein given this test is perfectly apt to be included amongst routine methods for laboratory diagnosis of Chagas disease.

H. Harold Scott

LEISHMANIASIS.

ANGEVINE D. M. HAMILTON T. R. WALLACE F. G. & HAZARD J. B. Lymph Nodes in Leishmaniasis. Report on 2 Cases. *Amer J Med Sci* 1945 July v 210 No 1 33-8 2 figs.

The two cases reported were in young soldiers of the U.S. Army who were admitted to hospital in England early in 1944 for enlargement of lymphatic glands particularly those of the cervical region. In both cases sections of glands removed by biopsy revealed leishmaniasis. In one case a sternal puncture failed to show any parasites in the second case sternal puncture was not performed. In both there was complete freedom from other symptoms or signs. Both were treated with sodium antimony gluconate solution one receiving a single dose of 6 cc. daily for 15 days and the other two such doses daily for seven days. It appeared that the infection in both cases had been

contracted in North Africa or Sicily during the latter part of 1943. Sections of the excised glands showed a moderate fibrosis of the capsule and the cortical lymph spaces filled with mononuclear cells and lymphocytes. The lymph follicles were relatively indistinct with considerable hyperplasia of the central parts. There was also a hyperplasia of the reticular network of the node. Throughout the pulp were focal areas of decreased cellularity, consisting of a spongy, oedematous stroma enclosing scattered histiocytes. Leishmania were found most frequently in such sites where there was a tendency to the formation of multinuclear giant cells in which parasites were present. Lymph nodes removed later showed that the spongy areas were infiltrated with and replaced by fairly compact sheets of pink staining epithelioid cells. In lymph nodes showing this reaction it was not possible to demonstrate parasites. It is thought that the histological features of the lymph nodes in these leishmaniasis infections should be of assistance in establishing a diagnosis and separating them from other chronic granulomatous conditions. It seems that the first of the two cases described in this paper is the one referred to in a paper by BURCHENAL and WOODS [this Bulletin 1945 v 42 635] C M Wenyon

SENEKJIE H A & LEWIS Ruth A. Diagnosis of Leishmaniasis by Slide Agglutination. *Proc Soc Exper Biol & Med* 1944 Oct v 57 No 1 17-19 [17 refs]

Sera were obtained by immunizing rabbits with 10 injections of 0.5 to 1.0 cc of killed cultures of *Leishmania brasiliensis*, *L. donovani*, *L. tropica* and *Trypanosoma cru* i [this Bulletin 1943 v 40 681]. After sera had been collected from the animals they were still further immunized by repeated injections of living cultures. From the flagellates slide agglutination antigen and H and O antigens were prepared. The various sera were tested against these three antigens. It was found that on the slide the homologous organism was agglutinated to a high titre but agglutination to a lower titre was obtained with the heterologous organisms. In all the flagellates tested H and O agglutinogens were present. It seems possible that a rapid diagnosis of visceral, cutaneous and muco-cutaneous leishmaniasis could be made by slide agglutination. C M Wenyon.

MACKAY DICK J. Comments on Kala Azar with a Report on Three Cases. *J Roy Army Med Corps* 1945 Aug v 85 No 2, 68-74

HARDY J D & PASSMORE, R. Kala-Azar as seen in an Indian Base General Hospital. *J Indian Army Med Corps* 1945 July v 1 No. 2, 26-8.

BATTELLI C, COCEANI A & ROSSI M. Ricerche sulla diffusione della leishmaniosi del Cane in Eritrea. [Incidence of Leishmaniasis in Dogs in Eritrea.] *Boll Soc Ital di Med e Igiena Trop* (Sez. Eritrea) 1944 v 4 No 3 497-505 [17 refs.] English summary (5 lines)

The authors have examined smears of the spleen and bone marrow of 86 dogs in Asmara, Eritrea, for evidence of leishmania infection. Parasites were discovered in eight of the animals. Various serological tests were also carried out. These were positive (+++ or +++) in most of the infected dogs but a small percentage of the apparently healthy animals gave a similar result. The various findings are set out in tabular form. Canine kala azar was previously recorded from Eritrea by COVATI in a dog in Ghinda (*Boll Soc Ital Med Col* 1931 p 170) C M Wenyon

FILTON J D Penicillin in *Leishmania* Infections. [Correspondence.]
Nature 1945 Aug 18 203

The author has treated hamsters experimentally infected with the parasites of Indian kala azar. They were treated daily over a period of eight days two with doses of 400 Oxford units administered intraperitoneally or subcutaneously every 3 or 4 hours and two with half this amount. There was no evidence that penicillin had any influence on the course of the infection. Tests were also carried out on the flagellate forms of *leishmania* in cultures. Here again penicillin even in high concentration was without any lethal action on the flagellates.
C M Wenyon

FERNÁNDEZ CASTAÑAS A. Nuevas aportaciones al tratamiento del kala azar infantil por el hexonato de antimonio en solución oleosa y concentrada. [Oil Suspension of Hexonate of Antimony in Treatment of Infantile Kala Azar. *Rev. Sanidad e Hig. Pública* 1945 Feb v 19 No 2 114-24 5 figs on 1 pl]

In an earlier communication (*Actualidad Médica* July 1943) the author reported on the successful treatment of two cases of infantile kala azar in Spain with the suspension in oil of the hexonate of antimony (sodium antimony gluconate) which was referred to in a paper by HIXUTH & SCHMIDT (this *Bulletin* 1944 v 41 194). In the present paper he reports on the treatment of seven other cases in children varying in age from 7 months to 3 years. The total quantity administered intramuscularly in each case varied from 10 to 19 cc. This quantity was given in 10 daily injections or in 7 injections on alternate days. In none of the cases was there any evidence of toxicity. The injections were well tolerated, and response as shown by cessation of fever reduction in the size of the spleen and improvement in the general health was rapid. There appeared to be every reason for assuming that a cure had been effected in all the seven cases. The author concludes that treatment with the oil suspension is the method of choice for cases of infantile kala azar.

The author at the end of his paper makes some remarks on the epidemiology of kala azar. He notes that Dr MORENO of Granada in a long experience of the disease has observed that in every case seen by him there has been a history of a previous case in the same house. It would seem that a reservoir of infection must exist. As in some cases there has been no association with dogs, cats or fowls, these animals cannot be implicated. It is suggested that the lizards (*Platydictylus mauritanicus*) may become infected by feeding on mosquitoes which have bitten the children. The mosquitoes again may convey infection from the reservoir lizards to the children. No experimental evidence in favour of or against this speculation is produced.
C M Wenyon.

FAROOQ M. & QUTUBUDDIN M. Oriental Sore in the Nizam's Dominions some Epidemiological Factors. *Indian Med Ga* 1945 Feb v 80 No 2 85-9 1 map 10 refs.

Oriental sore having been reported from time to time from Jalna and Pattan in the Aurangabad district in the most northern part of the Hyderabad Province the authors thought it worth while to make a careful survey of the population in these two towns as well as in Aurangabad. The populations of the three towns are—Aurangabad 50,924 Jalna 22,408 and Pattan 6,294. The incidence per thousand of oriental sore in most cases diagnosed by the

discovery of leishmania in the lesions in the samples of the population examined (1 032 3,242 and 1 781) was 4 84 27 76 and 42-68. The majority of cases were in children below the age of 10. Females appeared to be as commonly infected as males. Sandflies were most prevalent in Pattan where sanitation was very poor. The commonest species was *Phlebotomus papatasi* of which two specimens—one from Jalna and one from Pattan—showed flagellate infection of the midgut. *P. argentipes* was also taken in fair numbers while only a single specimen of *P. sergenti* was captured in Pattan. Three species or varieties of the *minutus* group—*P. antennatus*, *P. babu* and *P. bairyi*—were also represented.

C. M. Wenyon

LOPES C. F. & LAENDER J. F. A intradermo-reacção de Montenegro no diagnóstico da leishmaniose tegumentar Americana. Empregos de antígenos velhos—intradermo reacção negativa em casos de boubala. [Montenegro Skin Test in Mucocutaneous Leishmaniasis. Negative for Yaws.] *Brasil Medico* 1945 Feb 3 & 10 v 59 Nos 5 & 6 41-6 [10 refs.] English summary.

The authors carried out the Montenegro skin test in 50 cases of mucocutaneous leishmaniasis in Brazil employing as antigen a suspension in saline of killed culture flagellates of *Leishmania brasiliensis*. A reaction of at least 72 hours duration and of varying intensity was obtained in 92 per cent of the cases 48 of which were examined for the presence in the lesions of leishmania which were demonstrated in 24. In four cases there was a negative result in spite of the fact that leishmania were discovered in all. The four cases however were of cutaneous lesions only of not more than 6 months duration. In two of the cases a father and daughter the test was repeated twice with the same result. The reactions in cases with lesions of the mucous membranes were generally much stronger than in cases with cutaneous lesions only. The reaction was also more marked in cases of long duration. It was also positive in two cases which had been cured one and three years before. Tests were carried out with two samples of an antigen which had been stored in the ice box for one and four years. Both were found to be quite satisfactory a finding which is of importance to those who wish to keep stocks of antigen in more remote places. As controls 17 cases of other diseases including five cases of yaws were tested. All of these gave negative results. It is concluded that the Montenegro test as maintained by a number of earlier observers whose work is briefly reviewed is the method of choice for the diagnosis of mucocutaneous leishmaniasis in the clinics and health centres of the hinterland.

C. M. Wenyon

FEVERS OF THE TYPHUS GROUP

PROC. ROY. SOC. MED. 1945 July v 38 No 9 511-18 (Sect. Comp. Med. 21-8) 1 fig [28 refs.] Discussion on the Control of Rickettsial Infections [STUART HARRIS C. H. CARMICHAEL J. LEWTHWAITE R. PARISH H. J. (President) FULTON F. FELIX A. FOX L. A. LONGLEY E. O. HOLE N.]

This discussion held on April 18 1945 was opened by Lt. Col. C. H. STUART HARRIS who reviewed the whole subject of the prevention of typhus infection by delousing early diagnosis isolation and immunization by vaccines.

DDT was used for delousing great help was obtained from a rapid bedside slide test in which stained cultures of *Proteus OVI9* were employed. Since 1943 the vaccine used in the British Army has been prepared from yolk-sac suspensions purified by being extracted with ether according to the method introduced by Craigie in 1942.

The Naples epidemic, which in December 1943 looked like assuming disastrous proportions, was rapidly brought under control by searching for infected persons and dusting every possible "contact" with a 10 per cent DDT powder. The Allied Army Medical Officers Red-Cross workers and civilian personnel, were helped by workers of the International Health Division of the Rockefeller Foundation and of the American Typhus Commission at the height of the campaign as many as 60 000 persons were being deloused every day.

Dr J. CARMICHAEL referred to the tick borne rickettsial infection called heart water disease which occurs among cattle goats and sheep in South Africa. He said that the most effective method of prevention was by repeated arsenical dips for the destruction of the ticks. He also said that tick typhus in dogs might be of importance because of its possible transmission to man, but that it was easily controlled by applying derris pyrethrum, or arsenical washes to the dogs.

Mr E. O. LONGLEY described a fatal disease occurring among dogs in Nigeria. He thought that this was probably rickettsial, and he mentioned that he had suffered from an attack of typhus following a bite by a tick which was believed to have come from a dog. He added that previous cases of typhus fever in West Africa had been regarded as murine in origin, "probably on insufficient evidence." Dogs and other domestic animals even when they are susceptible to rickettsial infection, are not necessarily important reservoirs of the infection. They may serve chiefly as converters of ticks infected from wild animals.

Dr R. LEWTHWAITE gave a clear summary of modern knowledge of scrub typhus which in his opinion, ought to be called tsutsugamushi. He stressed the close relationship existing between this disease and the louse-borne flea-borne and tick-borne typhus fevers. Only the most expert pathologist could distinguish between the morbid anatomy and morbid histology of louse-borne and mite-borne typhus. His comments on mite-repellents mite poisons, and vaccine prophylaxis, were necessarily uninformative owing to the censorship still imposed on publication of the methods by which the disease was being successfully controlled. Flame throwers were mentioned as having been used with success in "civilizing" camp sites. Neither chemotherapy nor serotherapy had met with success. Many lives had been saved by nursing the patients "in situ" instead of sending them on a fatiguing journey to hospital. An example was given of the immunity that results from an attack of the disease among 28 workers deputed to graft palm trees in a highly infected area. There were 7 who had previously been patients in hospital and had been proved to be cases of scrub-typhus. All these remained healthy whereas 10 of the remaining 21 workers were attacked.

Dr Forrest FELTON said that when vaccines were standardized by counting the rickettsiae, it was found that yolk-sac and animal-lung vaccines gave similar degrees of protection. He suggested that the antigenic relationship between typhus rickettsiae and *Proteus OVI9* was heterologous.

Dr A. FELLIS suggested that serotherapy might be made more effective by adding anti-*Proteus OVI9* serum to anti-rickettsial serum because the latter is known to contain little of the heat-stable antigen which is an important element in producing immunity.

Brigadier General Leon A. Fox of the U.S.A. Typhus Commission said that he knew of no authenticated case in which a person vaccinated with the

Cox-Craig vaccine had afterwards died of typhus fever. He believed that when a large proportion of a population was vaccinated an epidemic could not get started and that an application of DDT rendered a person non-infestable for 3-4 weeks.

John W D Megaw

JETTAR, H M & SHIGAN LI Well-Felix Reaction of Men and Rats in Kweiyang. *Chinese Med J* * Washington. 1944 July Sept. v 62 No 3 227-30

In Kweiyang where a mild form of typhus fever occurs [see WU & CHU, this *Bulletin* 1945 v 42 795] the authors carried out agglutination tests on 352 sera sent for the Wassermann tests and on the sera of 349 rats. The reactions obtained are shown as percentages in the table —

Titre	Human Sera			Rat Sera		
	1-40	1-80	1-160	1-40	1-80	1-160 to 1-1,280
<i>Proteus</i> OX19	28.1	6.3	1.4	2.3	1.7	1.5
Pr OX2	5.1	1.7	0.6	3.2	0.6	0.6
Pr OXK	11.4	4.8	1.1	10.9	4.9	2.4
<i>Bact typhosum</i>	47.3	21.0	6.8		Not done	

Pregnant rats showed a much higher percentage of positives than the others; very young rats were seldom positive. In 37 rats *Trypanosoma lewisi* were found, and in 18 *Grahamella muris* in both of these groups a high percentage gave positive reactions against *Proteus* strains.

[No other figures are given in connexion with these interesting findings.]

Rats immunized against Pr OX19 showed a considerable degree of para-agglutination for OXA but very little for OX2. Rats immunized against OXA agglutinated OX19 almost as strongly as OXA.

The authors state that clinically the disease in Kweiyang does not suggest the severe classical type so it may be considered to be of the murine type.

[The severity of louse-borne typhus is so variable that it is a very unreliable differential diagnostic feature.]

John W D Megaw

COHEN S S The Chemical Alteration of a Bacterial Surface, with special reference to the Agglutination of *B. proteus* OX-19. *J Exper Med* 1945 Aug 1 v 82 No 2 133-42 4 figs [15 refs.]

The author has employed microelectrophoresis in the investigation of the agglutinins concerned in the Well-Felix reaction. He has applied this method in studying the effect produced by the addition of benzene sulphonyl chloride to cultures of *Proteus* OX19 and has presented a number of hypotheses as possible explanations of the effects observed.

The work is of a highly technical nature and will be of interest only to investigators into the antigenic structure of organisms used in agglutination tests. The author points out that Pr OX19 has at least two antigenic groups, one of which reacts with agglutinins contained in typhus serum, the other with agglutinins produced in *Proteus* infections, not necessarily of the OX19 type, so that the Well-Felix reaction is not absolutely diagnostic of either of these infections.

Even with rickettsia-agglutination reactions the differential diagnosis of epidemic and murine typhus is complicated by the complex nature of the antigenic structure of the rickettsiae.

John W D Megaw

DDT was used for delousing great help was obtained from a rapid bedside slide test in which stained cultures of *Proteus OVI9* were employed. Since 1943 the vaccine used in the British Army has been prepared from yolk-sac suspensions purified by being extracted with ether according to the method introduced by Craige in 1942.

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antigen it was found that the rickettsial agglutinins were still intact but after absorption with murine rickettsiae both the *Proteus* and murine agglutinins were removed.

Sera from 40 murine typhus patients 20 of which were tested singly and 20 others in one pool were completely negative with the R M-S-F R-A test and sera of rabbits which had been hyperimmunized with Rocky Mountain spotted fever rickettsiae did not agglutinate typhus rickettsiae. The rickettsia agglutination reactions in these diseases appear therefore to be fully specific. The author remarks that this finding is opposed to the results reported by Plotz *et al* [this *Bulletin* 1945 v 42 636] who found that sera from 13 of 14 cases of Rocky Mountain spotted fever agglutinated typhus rickettsiae. The report by Plotz is also said to be at variance with unpublished observations in this laboratory on the sera of spotted fever cases and is therefore puzzling.

The test is regarded as a simple method of detecting typhus infection in a rat population and as being particularly useful in the diagnosis of mild cases of human typhus. Murine and epidemic strains can be differentiated from each other and from Rocky Mountain spotted fever. The test may also be the only available means of diagnosing mild or inapparent infections in guinea pigs.

[The discordant results obtained by leading experts in connexion with the Rickettsia-agglutination reaction in cases of Rocky Mountain spotted fever will cause disappointment to those who hope for a simple and truly specific test by which to differentiate between the various fevers of the typhus group. The author's findings might even encourage clinicians to dream that one day they may be provided with sets of standardized rickettsial suspensions by which rapid slide tests could be employed for this purpose. This dream might still come true if it should turn out that the author's method of preparing the suspensions has eliminated a disturbing factor responsible for the occurrence of non-specific agglutination.] Presumably Plotz used rickettsial suspensions purified by repeated washing and centrifugation. According to WERTMAN [see this *Bulletin* 1945 v 42 635] relatively crude yolk-sac suspensions contain appreciable quantities of non-specific antigen capable of causing false positives in the highly sensitive complement fixation technique employed by Plotz who therefore purified his suspensions as stated above. The ether purification method introduced by CRAIGIE for the preparation of improved typhus vaccines [see STUART HARRIS above] may turn out to be more suitable for the production of highly specific suspensions for the rickettsia agglutination tests.

John H D Megaw

BENGTSON Ida A Applications of the Complement-Fixation Test in the Study of Rickettsial Diseases. *Amer J Pub Health* 1945 July v 35 No 7 701-7

The author summarizes and brings up to date the results of her very extensive work on the complement-fixation test as a method of diagnosis in Rocky Mountain spotted fever endemic and epidemic typhus fevers.

Among 216 sera giving positive fixation for Rocky Mountain fever 92.1 per cent had no cross fixation for endemic typhus antigen 3.7 per cent gave slight cross fixation and 4.1 per cent gave cross fixation at titres ranging from 1-32 to 1-256 but these titres were always much lower than those obtained with Rocky Mountain antigen.

Among 114 sera positive for endemic typhus 80 per cent gave no cross fixation for Rocky Mountain fever 9.6 per cent gave slight cross fixation and 9.6 per cent gave cross fixation at titres of 1-16 to 1-11 024 here again the cross-fixation titres were much lower

FITZPATRICK, Florence K. Studies on Rickettsial Agglutination in Typhus.
J Lab & Clin Med 1943 July 1 30 No 7 577-88 [22 refs.]

Most of the rickettsial suspensions used in these investigations were prepared by thoroughly shaking collections of infected yolk sacs in bottles containing glass beads, adding formalized (0.2 per cent) normal saline to make a 20 per cent suspension which was kept at 2-5°C for 3-7 days and was shaken daily. The suspension was filtered through gauze and then extracted with an equal volume of ether in the cold. About 18 hours later the antigen was drawn off and phenyl mercuric nitrate was added to make a concentration of 1-50,000.

Serum dilutions were made in tubes. A measured drop of each dilution was placed separately on one of 12 hollows on a glass slide and an equal drop of rickettsial suspension was added to each drop of diluted serum. The slide was placed on moist paper in a Petri dish and kept for 5 hours in an incubator at 40°C. It was then kept overnight in an ice-box. The results were read with a low-power microscope ($\times 100$).

The following abbreviations are used:

M R A—Murine rickettsial agglutination. E R A—Epidemic rickettsial agglutination. R M S F R A—Rocky Mountain spotted fever rickettsial agglutination. and W F—Weil-Felix reaction (*Proteus* O 19).

Numerous sera from healthy persons were examined but no positive reactions occurred with any of the rickettsial suspensions. Among 155 sera from persons with a clinical history of typhus fever (presumably murine) within the previous two years 104 were positive with the M R A test at titres ranging from 1-20 to 1-1,280. In 58 of the 104 positives the W F reaction was negative or at a lower titre. In 18 the W F titres were higher than the M R A.

In two cases of laboratory infection with epidemic typhus in previously vaccinated persons the W F E R A and M R A titres began to rise on the 5th day in one case and on the 8th day in the other. In the former case the maximum E R A and M R A titres (1-160) were the same. In the latter the E R A titre was 1-640 and the M R A titre was 1-160.

Among the sera of more than ninety persons recently inoculated with epidemic typhus vaccine of varying potency only 6 showed E R A titres as low as 1-20 and only one was completely negative. All the sera yielding these poor responses were from persons who had received vaccine of low potency. The rest were positive in higher titre. The W F responses were insignificant in all the cases in which comparison could be made with the pre-vaccination titres.

Among sera from 23 naturally infected rats, 15 were positive with the M R A test and though most of these also reacted with the E R A test the titres were always lower. Only one of the sera was positive with the W F test.

Guinea-pigs inoculated with epidemic or murine rickettsiae showed a rapid rise in titre when tested with the homologous rickettsiae, often also when tested with heterologous rickettsiae, but usually at much lower titres. In one lot of 6 mice inoculated intraperitoneally with murine yolk-sac rickettsiae M R A titres of + to +++ 1-40 were reached by all within a week and 4 of the mice had similar titres for the E R A test. Another group of 6 mice inoculated intravenously with epidemic rickettsiae were completely negative with the M R A test and all reacted with the E R A test. Mice inoculated intraperitoneally with epidemic rickettsiae showed some cross agglutination for murine rickettsiae but always at a much lower titre than for epidemic rickettsiae so that there was evidence of a very distinct antigenic difference between the epidemic and murine strains.

Absorption tests were found useful in the differentiation of the strains. After repeated absorption of the sera of murine typhus patients by *Proteus*

antigen it was found that the rickettsial agglutinins were still intact but after absorption with murine rickettsiae both the *Proteus* and murine agglutinins were removed.

Sera from 40 murine-typhus patients 20 of which were tested singly and 20 others in one pool were completely negative with the R M S-F R A test and sera of rabbits which had been hyperimmunized with Rocky Mountain spotted fever rickettsiae did not agglutinate typhus rickettsiae. The rickettsia agglutination reactions in these diseases appear therefore to be fully specific. The author remarks that this finding is opposed to the results reported by Plotz *et al* [this *Bulletin* 1945 v 42 636] who found that sera from 13 of 14 cases of Rocky Mountain spotted fever agglutinated typhus rickettsiae. The report by Plotz is also said to be at variance with unpublished observations in this laboratory on the sera of spotted fever cases and is therefore puzzling.

The test is regarded as a simple method of detecting typhus infection in a rat population and as being particularly useful in the diagnosis of mild cases of human typhus. Murine and epidemic strains can be differentiated from each other and from Rocky Mountain spotted fever. The test may also be the only available means of diagnosing mild or unapparent infections in guinea-pigs.

[The discordant results obtained by leading experts in connexion with the Rickettsia-agglutination reaction in cases of Rocky Mountain spotted fever will cause disappointment to those who hope for a simple and truly specific test by which to differentiate between the various fevers of the typhus group. The author's findings might even encourage clinicians to dream that one day they may be provided with sets of standardized rickettsial suspensions by which rapid slide tests could be employed for this purpose. This dream might still come true if it should turn out that the author's method of preparing the suspensions has eliminated a disturbing factor responsible for the occurrence of non-specific agglutination.] Presumably Plotz used rickettsial suspensions purified by repeated washing and centrifugation. According to WERTMAN [see this *Bulletin* 1945 v 42 636] relatively crude yolk sac suspensions contain appreciable quantities of non-specific antigen capable of causing false positives in the highly sensitive complement fixation technique employed by Plotz who therefore purified his suspensions as stated above. The ether purification method introduced by CRAIGIE for the preparation of improved typhus vaccines [see STUART HARRIS above] may turn out to be more suitable for the production of highly specific suspensions for the rickettsia agglutination tests.

John W D McGraw

BENGTSON Ida A Applications of the Complement Fixation Test in the Study of Rickettsial Diseases. *Amer J Pub Health* 1945 July v 35 No 7 701-7

The author summarizes and brings up to date the results of her very extensive work on the complement fixation test as a method of diagnosis in Rocky Mountain spotted fever endemic and epidemic typhus fevers.

Among 216 sera giving positive fixation for Rocky Mountain fever 92.1 per cent had no cross fixation for endemic typhus antigen 3.7 per cent gave slight cross fixation and 4.1 per cent gave cross fixation at titres ranging from 1-32 to 1-256 but these titres were always much lower than those obtained with Rocky Mountain antigen.

Among 114 sera positive for endemic typhus 80 per cent gave no cross fixation for Rocky Mountain fever 9.6 per cent gave slight cross fixation and 9.6 per cent gave cross fixation at titres of 1-16 to 1-11 024 here again the cross fixation titres were much lower.

Among 322 sera tested also by the Weil-Felix reaction 23.9 per cent. were positive with the complement-fixation test and negative with the Weil-Felix test: this finding occurred in 49 cases of Rocky Mountain spotted fever and in 28 of endemic typhus. In certain cases there was a positive Weil-Felix reaction and a negative complement fixation but in these cases a later fixation test usually gave more definite results and in cases of persistent divergence the possibility of *Proteus* infection has to be considered.

The long persistence of the complement-fixation reaction is a valuable feature: it often facilitates a retrospective diagnosis. The test was also found very valuable in detecting infection among rats: among 1,362 sera of rats from areas where endemic typhus occurred 48.7 per cent. were positive with the fixation test and only 3.6 per cent. with the Weil-Felix test. The fixation test is highly specific: several hundred normal sera, 150 sera of atypical-pneumonia patients and 40 sera found positive for tularemia, undulant fever or typhoid fever were negative for endemic typhus. Reactions at titres of 1-4 can therefore be regarded as significant.

When specific antigens become generally available say in the form of vaccines the test may become a routine procedure complementary to the Weil-Felix test.

John W D Megaw

LEÓN A P. Fijación del complemento por el suero de enfermos de tifo exantemático al *Proteus* OX-19 [A Complement Fixation Test for Exanthematic Typhus, using *Proteus* OX19] *Rev Inst Salubridad y Enfermedades Trop. Mexico*. 1945 Mar v 6 No 1 15-30 2 graphs. English summary.

Using an antigen prepared by a special technique from cultures of *Proteus* OX19 the author has tested the sera of 84 patients by the complement fixation method: the titres in 84 cases were 1-80 to 1-81,920 whereas by the Weil-Felix test 79 of the patients reacted at titres of 1-80 or over.

In 238 healthy controls the reaction was negative in 92 per cent. and the highest titre observed was 1-160. From one of the tables it appears that among the sera of 37 typhoid patients three were positive: 1/320, four showed a titre of 1-160 and two a titre of 1-80.

The reaction was found more sensitive than the Weil-Felix test especially during the early days of the illness. There was a close degree of correlation between the titres of fixation and the Weil-Felix titres.

Contradictory findings by other workers are attributed to differences in the methods of preparing the antigen: after failures with other methods the author hit on a technique which he describes in detail: he insists that this must be followed exactly if good results are to be obtained. The cultures were suspended in distilled water, concentrated by centrifugation, resuspended in distilled water shaken in a vessel containing glass balls and preserved by the addition of phenol and sodium chloride.

A curious finding was that the sera of 14 healthy rabbits reacted at titres of 1-120 to 1-600 and that no increase in these titres resulted from inoculation with *Rickettsia prowazekii*. Among guinea-pigs found negative before inoculation with *R. prowazekii* 60 per cent. became positive afterwards.

John W D Megaw

DE LA CAMARA J P. Observaciones sobre un brote de tifo exantemático en Madrid (Toledo) [Observations on an Outbreak of Exanthematic Typhus Fever in Madrid (Toledo)] *Rev Sanidad e Hig. Pública* 1944 Dec v 18 No 9 653-60 2 graphs.

In this outbreak 43 persons were attacked between November 1942 and April 1943. The source of infection was not discovered, and as the first case

was atypical infection had already spread before the nature of the disease was recognized.

In 34 of the cases contact with another patient was known to have occurred within the limits of the incubation period but in several cases the latest contact had been a month or more previously the author assumes that an inapparent attack must have intervened to maintain the chain of infection. Less than half of the attacks were typical the others were mild and might easily have been mistaken for influenza especially as no rash could be detected. All the attacks in children under 15 years of age were atypical and one inapparent case was detected by the occurrence of a positive Weil Felix reaction.

Sera from 38 patients were tested of these 31 reacted with *Proteus* O119 33 with *Pr* O12 and 33 with a strain supplied as *Pr* O1A but found to be different. All the sera reacted with one or more of these strains 27 reacted with all three and the average titre with O12 was higher than that with O119.

[These findings like many others suggest that the agglutinating properties of the strains used by different workers in carrying out the Weil Felix test are liable to considerable variations. There is a great need for standardized suspensions and uniformity in technique if the findings of different observers are to be comparable.]

John W. D. Megaw

GIROLD P & PANTHIER R. Comportement du rat à l'inoculation péritonéale de virus historique passé par lapin (souche pulmonaire lapin) (The Response of the Rat to Peritoneal Inoculation of Historic Virus passed through the Rabbit (Rabbit-Lung Strain)) *Ann Inst Pasteur* 1945 July-Aug. v. 70 Nos 7-8 248-9

The authors have already shown [this *Bulletin* 1945 v. 42 104] that historic strains of typhus rickettsiae might behave either as orchitic or non-orchitic strains according to the conditions in which they were transmitted by intra-peritoneal inoculation through guineapigs. When suspensions of infected rabbit lung were used to initiate the transfers through guineapigs and further passages were made with mixtures of vaginal exudate and spleen substance orchitis was produced up to the eighth passage but when brain substance was used no orchitis was produced.

In the present experiments three strains of historic rickettsiae which had been carried through 60 or more rabbit lung passages were used in attempts to transmit infection through rats by intraperitoneal or lung inoculation. There was complete failure to adapt any of the strains to passage through rats even when massive doses of rabbit lung substance were used to initiate the passages and even when the passages were initiated by vaginal exudate obtained from guineapigs of the fourth or fifth intraperitoneal passage—the initial guineapig passage having been made with infected lung substance of rabbits at the 80th or later lung passages. Mouse-lung substance was used in one experiment a mouse at the 88th lung passage was the source of the infected material the result was the same as when rabbit lung was used.

The authors conclude that the rat is a sure test for the differentiation of the historic virus and the murine virus.

From the details supplied by the authors it appears that a few of the rats primarily inoculated intraperitoneally with massive doses of infected lung substance died within three days some rats yielded a few rickettsiae from the vaginal exudate but in most cases no rickettsiae were found and the infection could not be maintained by further passages.

In the attempts to carry out lung passages through rats febrile reactions occurred—in one case up to the fifth passage—but no rickettsiae could be detected after the initial passage.

John W. D. Megaw

DE MAGALHÃES O & ROCHA, A. Contribuição para o conhecimento do tifo exantemático neotrópico no Brasil. [Contribution to the Study of Typhus in Brazil.] *Mem. Inst. Oswaldo Cruz* 1944 Feb v 40 No 1 1-8.

The authors describe the effects of the inoculation intraperitoneally into certain wild animals of suspensions of tissue of the central nervous system of guinea-pigs infected with a strain (VB) of Brazilian exanthematic typhus. The animals used were the coati (*Nasua narica*) a species of wild cat (*Felis wiedii*) a species of ferret (*Orison cillatus*) and a species of armadillo (*Tatus novemcinctus*). These animals got an inapparent infection: their blood gave positive Weil-Felix reactions and the presence of circulating virus was demonstrated by inoculation of their blood into guinea-pigs which became infected.

Some points in regard to Brazilian exanthematic typhus in man are mentioned: fever is often absent and the same applies to infections of susceptible animals whether with the active virus VB or the attenuated viruses VA1 and VA2. Splenomegaly is a much more important symptom of the infection than fever. The authors classify the clinical forms of the disease in man into inapparent, benign, grave and fulminating types: the grave type is further subdivided into the common grave form, the nervous or meningo-encephalic form and the uric form. They have seen very similar petechial rashes in Brazilian exanthematic typhus and typhoid fever and think that this similarity has led to confusion in the past.

J. F. Corson

BIRGER E. & BRZDZINSKI S. Die Inaktivierung des Fleckfiebertvirus durch Organextrakte und Fettsäuren. [Inactivation of the Virus of Typhus Fever by Extracts of Organs and by Fatty Acids.] *Schweiz. med. Woch.* 1945 June 23 v 75 No 25 568-70 [11 refs.]

The authors have demonstrated that pronounced antitoxic and antirickettsial effects are produced in mouse-lung suspensions of murine and classic typhus rickettsiae by the addition of (a) an extract obtained from healthy guinea-pig liver by a fat-solvent [Petrol ether], (b) cod-liver oil, (c) oleic acid and (d) vitamin F.

These effects were demonstrated by mixing each substance with a virulent suspension which after a suitable interval was used for the intraperitoneal or intranasal inoculation of mice. Suspensions treated with appropriate doses of each of these substances were much less lethal than similar quantities of untreated suspensions. Some examples are:—Among 10 mice inoculated intraperitoneally with 1.0 cc. of a 1-40 mouse lung suspension to which 10 mgm. of liver extract had been added 90 minutes previously, there were 4 deaths 2-14 days after inoculation, and among 20 mice inoculated with the same dose of untreated suspension there were 10 deaths within 24 hours and 8 deaths after 2-14 days. The liver extract was believed to be a fatty acid. In a similar experiment in which the suspension was treated with cod liver oil 45 minutes before the inoculation of 20 mice there were 4 deaths within 24 hours and 5 within 2-14 days: all the 20 control mice died within 12 hours. These experiments show that the substances had a pronounced antitoxic effect.

Suspensions treated with the liver extract were introduced by the nasal route into 30 mice of which 7 died after 5-7 days and one other at a later stage, whereas all of 13 control mice died after 3-4 days. In this case the infectivity of the suspension must have been greatly reduced by the liver extract.

When suspensions treated with oleic acid were used for nasal and intraperitoneal inoculation similar effects were observed.

The addition of "vitamin F" an unsaturated fatty acid to suspensions had a striking effect: none of 20 mice inoculated by the nasal route with suspensions containing 2-10 mgm. per cc. of the vitamin died, but all the 10 control mice died after 3-4 days.

When mice already infected by the nasal route were treated by considerable doses of oleic acid administered by inhalation no significant therapeutic effect was observed so that no claim is made for the efficacy of the drug *in vivo* despite its pronounced action *in vitro*

John H. D. Megaw

SNYDER J. C. & WHEELER C. M. The Experimental Infection of the Human Body Louse, *Pediculus humanus corporis* with Murine and Epidemic Louse-Borne Typhus Strains. *J. Exper. Med.* 1945 July 1 v. 82 No 1 1-19 3 pls. [23 refs.]

The authors give a detailed description of methods by which they have infected lice with typhus rickettsiae and have maintained the lice after infection by using rabbits for both purposes these methods obviate the necessity for intrarectal inoculation of the lice and the use of human beings for maintaining the infected lice

Groups of lice from colonies found free from rickettsiae were infected in two ways (a) by feeding them on a bleb produced by injecting a small quantity of infected material into the skin of the abdomen or ear of the rabbit and (b) by feeding them on rabbits which had received intravenously large doses of infected material usually yolk-sac suspensions The lice were maintained by feeding them on the skin of a rabbit after shaving it without the use of soap and then applying a little human saliva preferably from a non-smoker

Eight sets of experiments are described three of these were by the bleb technique four by the intravenous technique and one by both combined

Various materials from infected gerbils or yolk sacs mixed with human serum were used for the bleb technique 93 lice were used and the calculated rate of survival of the lice for 10 days after feeding was 48 per cent The routine test for infection was by examining gut smears for rickettsiae in each set of experiments the finding was confirmed by animal inoculation No infection was found during the first two days but the lice examined after 3 and up to 10 days had an infection rate of 76 per cent

For the intravenous tests 1174 lice were used the calculated survival rate was 23 per cent after 7 days Among the lice fed on rabbits less than 15 minutes after inoculation the infection rate was 98 per cent examples of the infection rates among lice fed at longer intervals are —After $\frac{1}{2}$ hour 93 per cent after 8½ hours 68 per cent after 45 hours 33 per cent and even after 93 hours 5 per cent No infection was found after 117 hours

Control lice fed on healthy rabbits never showed rickettsiae their 7-day survival rate was 95 per cent

In a separate experiment 2000 lice were fed on an infected rabbit within one hour by a single worker who also continued to feed all the surviving lice twice daily for seven days The faeces of the lice were infective for gerbils and in a random lot of 20 lice rickettsiae were found in 18 The worker who handled this lot of lice did not become infected he used rubber gloves and a mask two other workers who took no special precautions while handling infected lice had mild attacks

It is suggested that if proper precautions are taken lice may be used for the isolation of rickettsiae from patients

Epidemic strains of rickettsiae were used in all the above experiments except one in which seven lice were fed on a bleb infected with murine rickettsiae of the Wilmington strain obtained from tunica washings from an infected gerbil Five of the lice fed on the murine strain were injected into a guinea-pig which reacted with fever lasting three days and with scrotal swelling smears from the only louse tested in this way contained no definite rickettsiae

The original paper illustrated by five clear photographs must be consulted for details of the technique employed.

John W. D. Megaw

LYSKIS D. I. [A Case of Post Transfusion Typhus.] *Sovetskaya Medicina*. Moscow 1944 Nos 10/11 19 [In Russian]

The recipient was a woman who 10 days after operation for mastoiditis received a transfusion of 200 cc. citrated blood. Exactly 8½ days later she became febrile and 3 days afterwards developed a rash and the diagnosis of typhus was made. The donor of this blood was a woman who on the third day after the blood had been taken developed symptoms which later led to the diagnosis of typhus. This proves that the rickettsiae of typhus are present in the blood in the later stage of the incubation period.

H. N. Swann

ALCANTARA A. G. Formas clínicas del tifo exantemático. [Clinical Forms of Exanthematic Typhus.] *Rev. Sanidad e Hig. Pública* 1945 Jan. v 19 No 1 50-68 1 graph [25 refs.]

The author saw about 100 cases of house-borne typhus in hospital and private practice in Murcia between March 1941 and April 1944.

The rash never extended to the palms of the hands and it was seen on the face in only one case. The author found that the rash could often be detected at an earlier stage than usual by applying a dry cup for 6-8 minutes to the skin of the abdomen near the umbilicus. The rash was always macular never papular: when petechiae occurred they were situated in the centre of the macules.

The classification of the cases according to the main features was—cerebral (44) respiratory (9) digestive (7) mixed types (26) and typhus without rash (14).

The respiratory cases were often wrongly diagnosed as influenza pneumonia till the appearance of the rash indicated the real nature of the illness. The condition was regarded as a true typhus pneumonia caused by the rickettsiae: it did not yield to sulphonamides.

The digestive cases usually had diarrhoea with tenesmus and colicky pains in the umbilical region: they were usually rather mild and the termination was by slow lysis.

Among the cases without rash 11 were mild including three inapparent attacks in infants, and three were exceptionally severe.

The author accepts the view that attacks among children, which are often exceptionally mild and likely to be missed, are of great importance in maintaining the infection in a community: especially as lice infected from these patients tend to survive for long periods and so remain capable of transmitting infection far longer than severely infected lice.

John W. D. Megaw

DE MAGALHÃES O. & ROCHA, A. Tifo exantemático neotrópico no Brasil. Ensaio terapêutico com a Penicilina. [Typhus in Brazil. Therapeutic trial of Penicillin.] *Mem. Inst. Oswaldo Cruz* 1944 Aug. v 41 No 1 59-64. English summary.

"The authors described the experiments with Penicillin Merck Sodium Salt n. 135 in order to verify the curative action on the experimental disease of the guinea-pig.

1. They found that small doses of 1,600 units Oxford, when inoculated during the first 24 or 48 hours of the appearance of the feverish reaction are impotent to modify the course of the disease whether in the thermic curve or the testicular or splenomegaly manifestations.

2. Penicillin when used in larger doses, from 25 000 to 30 000 Oxford units in 24 hours through peritoneal cavity is capable of normalising the temperature modifying to a certain degree the virulence of the virus in the guineapig

3 In large doses even when injected later it causes the temperature to fall in all animals attenuating the visceral manifestations

4 Direct contact of Penicillin with the virus during many hours causes it to lose its virulence

They conclude that it is possible perhaps with stronger doses of the drug given intravenously in man to better the morbid evolution of the serious forms of Neotropic Exanthematic Typhus in Brazil not forgetting the death rate of the patients is from 85 to 100 per cent

YARYGIN N E & NAGIBINA N I [The Treatment of Typhus by Buxation, *Sovetskaya Meditsina* 1944 No 10/11 17-19 In Russian]

Buxation [a Russian term] is a form of irritation of the central nervous system, and consists in repeated withdrawal and reinjection of cerebrospinal fluid through a cerebrospinal [suboccipital?] puncture a 10 cc syringe is used and 10 cc. of cerebrospinal fluid is alternately withdrawn and injected 10 to 15 times the last syringeful not being reinjected. The method was used in cases of typhus of 5-8 days duration. On the day preceding the buxation the patient was given 10 doses of 0.6 gm. of sodium salicylate [orally?] and this was repeated on the day following the buxation. This treatment was given to 145 patients while another 20 patients received four doses of 0.5 gm. of sulphapyridine instead of sodium salicylate. The results are presented in four groups

I In 33 cases all symptoms disappeared immediately after buxation the temperature fell by crisis and the rash faded within two days there was no relapse.

II In 57 cases there was a more gradual disappearance of symptoms in about three days and no relapse occurred.

III In 18 cases symptoms disappeared as in Group II but some of the symptoms reappeared a very atypical form of typhus resulting

IV In 37 cases the treatment had no apparent effect

The fatality rate in the 145 cases treated with sodium salicylate was 3.45 per cent. which is half the rate observed in cases treated symptomatically. Complications were present in 8.9 per cent only. The other 20 cases were regarded as too few to enable an estimation of the effect of the treatment to be made. [The two queries in brackets were inserted to indicate that the original description was not quite precise.]

H W Swann

ALISOV P A. & KOSSOVAJA E M [Vaccine Therapy of Typhus,] *Sovetskaya Meditsina* Moscow 1944 Nos 10/11 15-17 [In Russian.]

Vaccine treatment was given in severe cases only in most of which complications were present and was not continued beyond the 8th-9th day of disease. The vaccine was diluted to one-fifth of the original strength and was injected intradermally. The first dose was 0.2 cc. divided and injected in two places. Doses were increased daily for the whole course of five days on the last of which 1.0 cc. was divided and injected in 10 different sites. In the whole course 3.0 cc. of diluted vaccine were used. There were some local, but no general, reactions in most cases a favourable effect was observed in that the fever began to subside and the rash did not become petechial. The average duration in patients treated with vaccine was 11.2 days, in controls 14.2. The mortality rate was only one third of that in the series of patients treated in the ordinary way

H W Swann.

NAI, K. & CARMICHAEL, M. R. *Streptococcal Infection in Laboratory Animals with Murine and Classic Typhus. II. Recovery of Strains. Proc. Soc. Exper. Biol. & Med.* 1945 Mar v 59 No. 1 84-8

The authors have already produced pneumonia in mice and rats by intranasal inoculation of a mixture of murine and *Leishmania* and have isolated themselves but both strains of infection persisted through several passages in the *Bull.* 1945, v 42, 457. They have now made a series of transfers through guinea-pigs by intraperitoneal inoculation starting with unknown organisms obtained from animals of the 1st passage of the mixed infection. Through male guinea-pigs 18 serial passages were made but only 2 of the animals had serum reactions. After a strongly positive complement fixation reaction the titres were considered a number when murine antigen was used then when classic antigen was used. Toxic material from the guinea-pig of the 12th passage was inoculated into female guinea-pigs which reacted weakly but after a few passages through female guinea-pigs (in which toxic material was used) there was a temporary increase in virulence. On transferring the infection again to male guinea-pigs the strain was found to give a weak swelling and to give a much stronger complement-fixation reaction with murine than with classic antigen.

A later series of transfers was made through female guinea-pigs starting with the same inoculating material as was used in the other series. In the 1st series the complement fixation reactions were broadly negative but in the 4th passage onwards reactions with classic antigen became strongly positive. Brain material from the female guinea-pigs when transferred to male guinea-pigs gave positive complement fixation reactions but after several further transfers through guinea-pigs some sera gave positive complement fixation reactions with classic antigen but none reacted with murine antigen.

It was concluded that transfers through male guinea-pigs favoured the production of murine rickettsiae and transfers through females favoured the production of the classic rickettsiae. (Jah II D)

the onset was 13.9 days. In the 13 previous cases treated in the same way but without atabrine the average duration was 16.2 days. The average duration of the fever after admission to hospital in the atabrine treated cases was 4.1 days; in the controls it was 6.2 days. The usual dosage was 0.1 gm. thrice daily.

The author states that the number of cases is too small to justify definite conclusions on the value of the drug but in the absence of any other available treatment he considers that its use is indicated.

Reference is made to the use of atabrin in the treatment of typhus fever by VAN MEERENDONK [this *Bulletin* 1943 v. 40 237] but in that series of trials also there were no real controls.

John W. D. Megaw

BLAKE F. G. MACEY H. F. SADUSA J. F. JR KOHLS G. M. & BELL E. J.
Studies on Tsutsugamushi Disease (Scrub Typhus, Mite-borne Typhus)
in New Guinea and Adjacent Islands. Epidemiology Clinical Observations,
and Etiology in the Dobadura Area. *Amer J Hyg* 1945 May v. 41
No 3 243-373 32 figs. (1 map) & 3 coloured pls [152 refs]

This important paper runs to 130 pages; it deals with a review of the literature (32 pages), epidemiology (20 pages), clinical observations (31 pages) and aetiology (33 pages); there is also a bibliography containing 152 references. There are 32 black and white illustrations and three plates containing good reproductions of colour photographs.

The investigation was carried out under the auspices of the U.S.A. Typhus Commission and the Preventive Medical Service of the U.S.A. Army. Independent investigations made by officers of the Australian and U.S.A. forces have been freely quoted and as reports of most of these have already been reviewed in this *Bulletin* the present abstract will deal chiefly with the unpublished work carried out by the authors.

In the critical review of the literature the following statements are made — (1) The name *Rickettsia orientalis* proposed by Nagayo in 1930 has the best claim to recognition. (2) the name tsutsugamushi has precedence over other designations of the disease. (3) the only species of mite hitherto proved by animal experiment to be a vector is *Trombicula akamushi* though there is much evidence to incriminate *Tr. deliensis* and (4) the only animals yet found naturally infected are the field vole *Microtus montebelloni* in Japan and an undetermined species of wild rat in the Federated Malay States.

The authors investigated the mites of the Dobadura area of New Guinea and isolated *R. orientalis* from two pools of *Tr. fletcheri* each of which was collected from a separate bandicoot (*Echymipera cockerelli*); neither of the bandicoots showed any evidence of being infected though a thorough investigation was made. A few *Tr. deliensis* and *Tr. walchi* [see KOHLS *et al* below] were found; the former only in one restricted area which happened to be highly infected; the latter occurred sparingly. Among 13 other species of mites found in the area *Tr. buloensis*, *Schöngastia blastover* and *S. pusilla* were abundant and widely distributed; they were known to attack man and to cause scrub itch but it seemed quite unlikely that they served as vectors.

The clinical features of 20 proved cases of mite-borne typhus were investigated; there were two deaths: one patient died suddenly and unexpectedly on the 5th day of a haemorrhage in the pons and medulla, the other was one of the two patients who had hepatitis with jaundice. The severity was very variable ranging from mild (two cases) to severe or very severe (nine cases). There were clinical signs of pneumonitis in 13 cases; in seven of these the condition was severe but it was regarded as being essentially rickettsial in origin except in one patient from whom a pneumococcus was recovered.

SILVA, R. & CASTAÑEDA, M. R. Simultaneous Infection in Laboratory Animals with Murine and Classic Typhus. II. Recovery of Strains. *Proc. Soc. Exper. Biol. & Med.* 1945 May v 59 No 1 84-6.

The authors have already produced pneumonia in mice and rats by intranasal inoculation of a mixture of murine and classic rickettsiae and have satisfied themselves that both strains of infection persisted through several passages (see this *Bulletin* 1945 v 42, 457). They have now made a series of transfers through guinea-pigs by intraperitoneal inoculation, starting with mouse lung suspensions obtained from animals of the 10th lung passage of the mixed infection. Through male guinea-pigs 18 successive passages were made all but two of the animals had scrotal reactions - all gave strongly positive complement fixation reactions the titres were considerably higher when murine antigen was used than when classic antigen was used. Tissue material from the guinea-pig of the 10th passage was inoculated into a female guinea-pig which reacted feebly but after a few passages through female guinea-pigs (in which brain material was used) there was a temporary increase in virulence. On transferring the infection again to male guinea-pigs the strain was found to cause scrotal swelling and to give a much stronger complement-fixation reaction with murine than with classic antigen.

Another series of transfers was made through female guinea-pigs starting with the same mouse-lung material as was used in the other series - in the early passages the complement fixation responses were feeble or negative but from the 4th passage onwards reactions with classic antigen became strongly positive. Brain material from the female guinea-pigs, when transferred to males, caused no scrotal reactions but after several further transfers through male guinea-pigs some sera gave positive complement fixation reactions with classic antigen, but none reacted with murine antigen.

It was concluded that transfers through male guinea-pigs favoured the isolation of murine rickettsiae and transfers through females favoured the preservation of the classic rickettsiae.

John W. D. Megaw

DAMON, S. R. & JOHNSON, Mary B. The Serologic Diagnosis of Endemic Typhus. II. A Comparison of Water-Bath and Icebox Fixation in the Complement Fixation Test. *J. Lab. & Clin. Med.* 1945 May v 30 No 5 415-19 [10 refs.]

Using various antigens including a number of commercial epidemic typhus vaccines, the authors have carried out a series of complement fixation tests on the sera of rats infected with endemic typhus. They followed the technique described by BENGTSON [this *Bulletin*, 1944 v 41 738] but found that by keeping the mixtures of serum, antigen and complement in the icebox overnight much higher titres were obtained than when the mixtures were incubated for one hour at 37°C. Many human sera were also tested, with similar results and in some cases weak positives were obtained with the icebox technique when the results with the other method were negative. In these cases later tests yielded high-titre reactions with both methods but the titres were always higher with the modified technique.

The authors consider that the method is likely to be of special value in rat surveys of localities in which endemic typhus is suspected.

John W. D. Megaw

ARBONA, G. Atabrine in the Treatment of Endemic Typhus Fever. *Bol. Asoc. Med. de Puerto Rico.* 1945 June v 37 No. 6 208-10 3 charts.

The average duration of the fever in 13 cases of endemic flea borne typhus fever in which treatment by atabrine [mepacrine] commenced 5-19 days after

modern developments in connexion with preventive measures which for obvious reasons could not be discussed at the time of writing.]

John W. D. Megaw

BLAKE F G MAXCY K F SADUSA J F JR KOHLS G M & BELL, E J
Trionbicula fletcheri Womersley and Heaslip 1943, a Vector of Tsutsu-
gamushi Disease (Scrub Typhus) in New Guinea *Science* 1945 July 20,
61-4 [Refs in footnotes]

This is a preliminary notice of the work reviewed above

KOHL G M ARMSTRIST C A IRONS E N & PHILIP C B Studies on
Tsutsugamushi Disease (Scrub Typhus, Mite-borne Typhus) in New Guinea
and Adjacent Islands Further Observations on Epidemiology and Etiology
Amer J Hyg 1945 May 41 No 3 374-96 14 refs.]

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In one area in Dutch New Guinea a single regiment had 308 admissions including the Officer Commanding and 30 other officers. In two islands off Dutch New Guinea there were 1 056 cases within 2½ months and one-quarter to one third of the personnel of three battalions were attacked. The case-fatality rate varied from less than 1 per cent to 27.5 per cent.

In the Dobadura area more than 30 species of mites were found. 65-72 per cent of all the mites found on rats and bandicoots in this area were *Trionbicula fletcheri* which were very abundant on the animals in grassy areas but fewer in those found in jungle and well-cleared camp sites.

Details are given of the mites found and of their vertebrate hosts which included birds. A few ticks were found in one affected area: a single *Amblyomma* (species not identified) was found on each of three men. Preliminary attempts to transmit infection by *Ornithodoros moubata* failed.

One strain of *Rickettsia orientalis* was recovered from a pool of *Tr. fletcheri* taken from a rat (*Kallus concolor browni*) and three other strains were recovered from *Tr. walchi* from rats of the same species. Altogether 56 pools comprising 17 000 mites were tested. It is strongly suggested that *Tr. walchi* may be the same as *Tr. deliensis* Walch.

Attempts were made to infect eight locally captured bandicoots by intra-peritoneal inoculation but without success. Among four other bandicoots from a non-infected area (Brisbane) inoculated in the same way three gave no reaction but peritoneal washings from the 4th animal were infective to mice though blood and brain substance of this animal was not infective. The authors comment that "this is an anomalous result without adequate explanation" and they regard bandicoots as being unlikely to be natural reservoirs of infection.

Among 36 pools of wild rats of various species comprising 102 rats *R. orientalis* was recovered from two pools made up of seven and four rats respectively, all belonging to the species *R. concolor browni*. Some of the rats in each of these two pools were infested by *Tr. fletcheri*. The rickettsiae were identical with those recovered from patients and mites as described in the preceding paper.

Altogether 30 strains of *R. orientalis* were recovered from patients: 15 from blood taken on the 3rd to the 10th day of the illness and 15 from heart blood obtained at autopsies.

The incubation period ranged from 10 to 18 days. An eschar was found in every case. The rash seldom extended to the face, feet or hands.

Among 24 cases in which the Weil-Felix reaction was studied there were seven in which the *Proteus* OVK titre never exceeded 1-40 and two others in which it was 1-80. In the remaining 15 it rose at some period to 1-320 or over though in no case examined between the 4th and 11th days was a titre higher than 1-40 observed. With *Pr* O1⁺ all the reactions were negative with *Pr* O119 5 were negative 5 were positive 1-20 7 were positive 1-40 4 were positive 1-80 and 3 were positive 1-160 but these reactions were not in rising titre and similar reactions occurred in 5 of 13 patients suffering from other diseases so also 3 of these 13 had titres of 1-40 against *Pr* OVK.

Problems in differential diagnosis arose in addition to the 20 patients in whose cases the diagnosis was confirmed eight patients with an initial diagnosis of the disease were studied but five of these turned out to be "proved" cases of dengue one was doubtfully dengue, and two others were infectious hepatitis. There was still another case in which the diagnosis remained doubtful after full investigation. In four of the cases of dengue the maximum OVA titre was 1-40 the rash in five of the cases of dengue and in one case of infectious hepatitis was not "clearly distinguishable from that of mite-borne typhus." [The evidence on which the diagnosis of dengue was regarded as proved is not stated.]

In 16 cases attempts were made to recover *R. orientalis* from the blood of patients by intraperitoneal inoculation of white mice. In four of these dengue was diagnosed in two others the diagnosis was infectious hepatitis and in another the diagnosis remained uncertain from the remaining nine patients the organism was isolated and thoroughly studied by repeated passage through mice which usually died between the 10th and 20th day after inoculation by the intraperitoneal route. Suspensions of blood or brain tissue of the mice, diluted 1-30 in the later passages were always infective they were taken on the 7th to the 14th day. Smears of peritoneal scrapings of the infected mice always showed rickettsiae. The primary inoculation of the mice was by 0.2-0.3 cc. of a 10 per cent suspension of blood clot in normal saline.

Intraocular inoculations with infected material from mice were carried out on 54 rabbits of which 49 reacted in the typical manner but none of the rabbits developed the positive OVA agglutinins described by LEWIS and WHITE as occurring in 50 per cent of rabbits inoculated by this route. All the six strains used for these inoculations gave positive results these are beautifully illustrated by six photographs in colour.

The Syrian hamster was found specially suitable for passage of the rickettsiae after intraperitoneal inoculation all the animals died but after subcutaneous inoculation most of them survived and so were valuable for immunity tests because of their being unsuceptible to intraperitoneal inoculation.

Yolk-sac cultures were successful in all the five strains that were tested great variations occurred in the number of rickettsiae seen in smears but the yolk sacs in which very few organisms were found were infective in the same extremely high dilutions as the sacs containing numerous rickettsiae.

The two strains isolated from mites were thoroughly investigated and were found to be identical with the human strains. Full details are given of all these laboratory studies by which the identity of all the strains was established most of the studies were carried out in the Division of Virus and Rickettsial Diseases of the Army Medical School Washington, after the return of the Commission to the U. S. A.

[This monograph will be found invaluable by all workers on mite-borne and other typhus fevers it deals with every aspect of tsutsugamushi disease except

modern developments in connexion with preventive measures which for obvious reasons could not be discussed at the time of writing.]

John W D Megaw

BLAKE F G MAXON K F SADUSK J F JR KOHL G M & BELL, E J
Trombicula fletcheri Womersley and Heatlip 1943 a Vector of Tsutsu-
gamushi Disease (Scrub Typhus) in New Guinea. *Science* 1945 July 20,
61-4 [Refs in footnotes.]

This is a preliminary notice of the work reviewed above

KOHL G M ARMBRUST C A IRONS E N & PHILIP C B Studies on
Tsutsugamushi Disease (Scrub Typhus, Mite-borne Typhus) in New Guinea
and Adjacent Islands Further Observations on Epidemiology and Etiology
Amer J Hyg 1945 May v 41 No 3 374-96 [14 refs]

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Altogether 30 strains of *R. orientalis* were recovered from patients: 15 from blood taken on the 3rd to the 10th day of the illness and 15 from heart blood obtained at autopsies.

Infection in guinea-pigs was non-orchitic and it tended to die out after a few passages. In white rats the infection was inapparent but it persisted for long periods in the brain in one case up to 83 days at least it caused no rise above 1-40 in the Weil-Felix titre in the rats.

Unsuccessful attempts were made to induce larval mites captured on animals to bite other animals so that mites attached to rats or domestic pets are not regarded as being "particularly hazardous" and as rats often persist in large numbers in places from which the disease has disappeared control measures should probably be concentrated on the mites. Repellents such as a 5 per cent. emulsion of dimethyl phthalate in 2 per cent soap solution have been found effective.

John W. D. Megarr

MACHIELLA, T. E. & FORRESTER, J. S. Mite or Scrub Typhus. A Clinical and Laboratory Study of 64 Cases. *Amer J Med Sci* 1945 July v 210 No 1 33-61 4 figs & 12 charts

The authors give an exceptionally clear and orderly description of the clinical features observed in 64 cases of mite-borne typhus during the last three months of 1943 and the first month of 1944. The patients were 40 Chinese and 24 American soldiers, all of whom had been in the jungle during the weeks immediately preceding the onset.

Only one of the patients died and no mention is made of any exceptional incidence of previous illness or severe hardship so that the clinical picture was not likely to have been seriously affected by these disturbing factors.

The authors state that in this paper the disease will be referred to as mite typhus, the name scrub typhus being reserved for those cases of typhus-like disease in which the vector is not reasonably clear. [The unhappy name scrub typhus is now so firmly established by usage as a synonym of mite-borne typhus that this special application of the term is not likely to be adopted.]

The average duration of the fever was 18.3 days in Chinese and 16 days in American patients. Of the onset symptoms cough and epistaxis were more frequent in the former and photophobia in the latter group otherwise no great difference was observed between the two groups. All the American patients had been inoculated against louse-borne typhus at unspecified dates but neither the severity of the attacks nor the Weil-Felix titres seemed to have been influenced by the vaccine.

The figures shown below in parentheses refer to percentage incidence.

The primary lesion (67) was usually on the upper part of the trunk, mostly in the axillae or on the left costal margin. It appeared first as a red macule which in a few days became a papule soon being replaced by an ulcer filled by a black eschar. In all but four cases the local lesion was accompanied by regional lymphadenitis. The onset was sudden though sometimes the temperature rose gradually the chief features being fever (90), anorexia (88), headache (76), chill (68), conjunctival injection (53), cough (40) and backache (25). Apathy was pronounced but the eyes were bright and alert as in louse-borne typhus.

The types of temperature curve were typhoidal, relapsing remittent or intermittent. One patient was regarded as having had a true relapse his temperature had become almost normal on the 12th day but on the 13th day it began to rise again though the fever continued to be remittent and there was a recurrence of splenomegaly. The total duration of fever was 24 days and the Weil-Felix reaction did not become positive till the 21st day of the disease.

The rash (51.5) was usually maculo-papular but sometimes it was purely macular the palms and soles were never involved. The spleen was palpable in 88 per cent of the Chinese patients and occasionally it was also tender. Generalized lymphadenopathy (93.7) appeared during the first week. Distension of the retinal veins was seen in 30 Chinese and 14 American patients about the 7th day it was followed by oedema of the optic disk in 18 Chinese patients of whom four developed retinal haemorrhages. Among the 40 Chinese patients X ray examination showed the presence of bronchitis in 9 of bronchopneumonia in 9 and of both these conditions in 4. The authors could not be certain whether the pulmonary involvements were complications or part of the disease [Probably the latter sulphadiazine was given to some of these patients without effect.] Acute mania occurred in one patient on the 7th day. Muscular twitchings were observed in 4 cases, generalized convulsions in 2 and meningismus in one patient whose spinal fluid contained 60 leucocytes per cmm. and a trace of globulin in this and two other cases the fluid was at high pressure.

Among 12 patients examined by electrocardiography one had indications suggesting myocardial damage. The Weil Felix reaction (with *Proteus OAX*) did not become positive till after the end of the 2nd week in 29.7 per cent of the Chinese patients in two cases not till the end of the 6th week. Titres exceeding 1-200 were observed in 15 of 25 patients who had primary ulcers and in only one of 15 who had no ulcer.

The leucocyte picture was very variable a moderate degree of leucopenia and a gradual increase in the percentage of lymphocytes were frequent findings. Mild or moderate azotaemia occurred during the 2nd or 3rd week in 13 of the Chinese and three of the American patients. The patient who died had appeared to be doing well except for a rapid rise in his blood urea nitrogen which reached 103 mgm. per 100 cc. on the 16th day when he suddenly had generalized convulsions with coma, soon followed by death in a state of shock.

In 19 Chinese and six American patients there was some degree of albuminuria with granular or hyaline casts in five cases a few red blood cells were found in the urine.

Treatment was mainly symptomatic and supportive and general measures included adequate intake of fluid and calories by mouth whenever possible. Sulphadiazine was given to 10 patients without obvious benefit. Convalescent blood given in a dose of 500 cc. to two patients on the 5th day did not appear to influence the course of the disease. Oxygen was given for cyanosis and blood transfusion for the shock state.

John W D Megaw

FISCHBACH W M & HOWELL, D E. Observations on Tsutsugamushi Disease
U.S. Nav. Med. Bull. 1945 Sept v 45 No 3 423-8 2 graphs.

BRAZAVILLE [A. E. F.] RAPPORT SUR LE FONCTIONNEMENT TECHNIQUE DE
L'INSTITUT PASTEUR EN 1943 [CECCALDI J. Director] 87-8 La
réaction de Weil Félix chez les chiens de Brazzaville. [The Weil Felix
Reaction in Dogs in Brazzaville.]

The sera of forty six dogs some of which belonged to Europeans who had recently had fever with a rash of the typhus type were tested against *Proteus* OX19 OX2 OXA and OYL. Positive results were found in seven 5 with OX19 at 1-50 4 with OX2 at 1-50 3 with OXA at 1-100 1 with OYL at 1-100.

It is concluded that infection of the *boutonneuse* type can stimulate in dogs agglutinins for the various strains of *Proteus*.

Charles Wilcocks

MILNE, R. I. A Note on the Incidence of Sandfly Fever in the Naval Camp at Haifa.
J Roy Nav Med Serv 1945 July v 31 No. 3, 179-80 1 graph.

FITZPATRICK Florence K. Penicillin in Experimental Spotted Fever *Science*
 1945 July 27 98-7

Each of six guinea-pigs whose average weight was about 500 gm. received 500 units of penicillin intramuscularly every 4 hours for 4 days the treatment began 48 hours after the onset of fever resulting from an intraperitoneal inoculation with a virulent strain of Rocky Mountain spotted fever rickettsiae. All the guinea-pigs died.

Six guinea-pigs inoculated in the same way received 10 cc. of spotted fever rabbit immune globulin 48 hours after the onset of the fever and all recovered.

Among 16 control guinea-pigs inoculated in the same way and receiving no treatment there were eight recoveries.

The penicillin-treated guinea-pigs showed all the typical reactions that follow inoculation with a virulent strain of the spotted fever rickettsiae and the higher mortality among the treated animals was probably due in part to the toxicity of the drug.

Estimates of the penicillin content of the plasma of the treated animals showed that the treatment would have been adequate if it had been of value the dosage corresponded to a total of 2 million units for a person weighing 160 pounds

John W D Mcgar

BARTONELLOSIS

LEBATTIA F & VIEIRA, G. Estudos sobre a bartonelose I A bartonelose dos ratos esplenectomizados e a Penicilina [Studies on Bartonellosis. I. The Effect of Penicillin on the Bartonellosis of Splenectomized Rats.] *Mens Inst Oswaldo Cruz* 1944 Aug v 41 No 1 21-44 8 figs. [35 refs. English summary]

The experiments the upshot of which is here related, were carefully carried out and though the result was negative it is none the less important. After reviewing published work on the anaemia of bartonellosis in rats the author proceeds to show that 95 per cent of the white rats at the Institute develop bartonellosis after splenectomy and that the fall in the haemoglobin coincides with the appearance of the *Bartonella* in the peripheral blood. This drop in the haemoglobin is more rapid than the reduction in red corpuscles, and when regeneration takes place the haemoglobin recovery is quicker than that of the corpuscles but death results in about half the animals, and haemoglobinuria is a bad prognostic sign. Attempts to ward off the fatal issue by the use of penicillin were ineffectual.

H Harold Scott

DENGUE.

KAPLAN A & LINDGREEN A. Neurologic Complications following Dengue
U.S Nav Med Bull 1945 Sept. v 43 No. 3 508-10

In a hospital in the Central Pacific, 1489 cases of dengue were seen within a period of 40 days. Soon after recovery—usually about two weeks but in

one case only three days and in another a month—13 of the patients had unilateral attacks of neuritis. The nerves affected were —The facial (Bell's palsy) in two cases the palatine long thoracic and ulnar in two cases each the peroneal nerve in four cases and the sciatic nerve in one case

Most of the patients were evacuated and could not be followed up but one of the patients who had Bell's palsy had recovered six weeks later in one case of palatine nerve palsy there was great improvement within three months and in one case of ulnar nerve palsy improvement was pronounced within two weeks. On the other hand no improvement had occurred in either of the cases of long thoracic nerve palsy after two and three months respectively and in the case of peroneal nerve palsy that could be followed up there was no improvement five weeks after the onset

The attack of sciatic neuritis began three days after recovery from dengue no improvement had occurred within three weeks.

All the patients were treated with thiamin though there was no reason to suspect vitamin deficiency all of them had received tetanus toxoid four to twelve months previously It was thought likely that other cases might have occurred

John W D Megaw

BACILLARY DYSENTERY

ROSE T F The Clinical Differentiation of Appendicitis and the Dysenteries.
Med J Australia 1945 July 21 v 2 No 3 72-7

The author has been impressed by the number of cases of acute appendicitis in the tropics in which diarrhoea is prominent and may resemble that of early bacillary dysentery

He has encountered cases of bacillary dysentery which simulate appendicitis. He further has had cases of amoebic dysentery which simulated appendicitis and on one occasion he found an obstructive appendicitis to be a sequel of a *Schistosoma japonicum* infection of the gut wall.

Detailed reports are given of 14 cases illustrating his points and he emphasizes the importance of carefully taken histories and (far more important) of careful physical and pathological examinations in order that errors in diagnosis may be avoided.

A R D Adams

MORTON H. E. & ENGLE Y F B Jr Dysentery Bacteriophage. Review of the Literature on its Prophylactic and Therapeutic Uses in Man and in Experimental Infections in Animals. *J Amer Med Ass* 1945 Mar 10 v 127 No 10 584-91 [46 refs.]

This is an excellent critical review compiled with the object of evaluating existing evidence relating to the prophylactic and therapeutic use of dysentery bacteriophage. It is itself a summary which should be read in the original. In adequate trials there must be bacteriological confirmation of all cases and the phage used must be shown to be potent *in vitro* against the infecting strain. Since dysentery mortality is low the best criterion of effectiveness is the time taken to clear the organism from the faeces. This test may be vitiated by the presence in the faeces of natural or administered bacteriophage which may inhibit the growth of dysentery bacilli in culture so that the formaldehyde method of KLIGLER *et al* [*Bulletin of Hygiene* 1943 v 18 950] should be used.

The authors examine nine reports which purport to show that dysentery phage is therapeutically ineffective in man. Discarding those trials in which the groups were too small to have scientific value or the control group was

inadequate or the bacteriological investigations were open to criticism, two reports are regarded as worthy of further consideration. One is a trial described by KESSEL and ROSE [this *Bulletin* 1933 v 30 762] who found in comparison with an untreated control group no significant difference in case-mortality or length of stay in hospital of bacteriologically confirmed cases of Flexner dysentery treated by a phage shown to be potent *in vitro*. The numbers are however too small and the suggested clearance test would have been a better criterion. The other trial is that of BOYD and PORTNOY in North Africa [this *Bulletin* 1944 v 41 569]. They found no significant difference in the percentage of their treated and untreated individuals who developed dysentery or required admission to hospital, and no difference in the duration of stools containing blood and mucus. The average stay in hospital of the treated group was 2.86 days less than the untreated group. The reviewers comment on the low titre of the phage used.

Of 19 reports which have been cited as evidence in favour of the therapeutic value of dysentery phage few many are able to withstand criticism for reasons similar to those noted above. The most extensive trial is that of MELNIK, KHAISOVITCH and NIKHONOV (*Ann. Bull. Melchinskoy Inst.* 1935 v 1 97) who observed a mortality of 1.4 per cent in 282 cases treated with Shiga phage compared with that of 2.3 per cent in 1,059 untreated controls. It was claimed that, of the treated cases, 55.3 per cent. left hospital within 4 days compared with 18.6 per cent of the control group. Bacteriological cure was however not determined so these results may indicate only alleviation of symptoms. These workers noted that recovery might be delayed in cases in which the dysentery bacillus was associated with *Proteus* or enterococci. This may be an important factor in the evaluation of treatment.

The verdict on the therapeutic value of bacteriophage in dysentery in man must therefore be "not proven".

In estimating the prophylactic value of dysentery phage it must, of course, be established that the phage which was used was active against the strains subsequently encountered. Four reports examined are regarded by the authors as showing that phage is capable of preventing bacillary dysentery in man. The most encouraging results were obtained by ASHESHOV *et al.* [this *Bulletin* 1931 v 28, 893], MELNIK, NIKHONOV and KHAISOVITCH (*Ann. Bull. Melchinskoy Inst.* 1935 v 1 89) and KLEWE and HELMREICH (*Munch. med. Woch.* 1941 v 89 617). Boyd and Portnoy [above] obtained less striking results in tests in which they used phage captured from the enemy on prisoners of war in North Africa.

The effect of phage on experimental dysentery infection in animals has been studied by a number of workers and during the past two years reports have been published by RAKIETEN and RAKIETEN (*J. Bacteriology* 1943 v 45 477), MACNEAL, BLEVINS and PACIS (*J. Bacteriology* 1943 v 46 111), DUBOS, STRAUSS and PIERCE (*J. Exper. Med.* 1943 v 78 181), MORTON and ENLEY (*J. Bacteriology* 1944 v 47 475) and MORTON and PEREZ-OTERO (*J. Bacteriology* 1944 v 47 475). These reports show without any doubt, that bacteriophage can take place *in vivo* and protect developing chick embryos and white mice against fatal infections with dysentery bacilli: that phage increases in amount *in vivo*; that it is not eliminated from the blood in 24 or 48 hours; and that quite small quantities are sufficient to have a protective effect.

The authors point out that it is illogical that tests in man were made before the animal experiments and they consider that a carefully planned prophylactic and therapeutic trial in human beings might now appropriately be made.

J. C. Crickshank.

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

BALAMUTH W & SANDZA J G Simple, Standardized Culture Medium for Physiological Studies on *Entamoeba histolytica* *Proc Soc Exper Biol & Med* 1944 Oct v 57 No 1 161-3

After various attempts to produce a simple easily prepared medium for cultivation of *E. histolytica* the authors have arrived at the following—Two eggs are boiled for 15 minutes after cooling the yolks are separated and crumbled in 125 cc of 0.8 per cent sodium chloride solution. The mixture is boiled for 10 minutes and after evaporated water has been replaced the infusion is filtered by suction. The filtrate is again brought to 125 cc. by addition of water and autoclaved for 20 minutes at 15 pounds pressure. After cooling the slight precipitate is removed by simple filtration. To the filtrate is added 125 cc of M/15 phosphate buffer (pH 7.5) making the total salt concentration M/30 phosphate solution in 0.4 per cent sodium chloride. The final mixture is distributed in test tubes in 5 cc amounts autoclaved and stored under refrigeration. Before a tube is inoculated with amoebae a loop of sterile rice starch is added to it. The sterile medium thus prepared is almost completely transparent. The growth of amoebae is uniformly good, the maximal growth being attained on the second to the fourth days and active amoebae persisting for more than nine days. Though the growth was not so intense as in some other media it was particularly suitable for studies in cellular biology. Better growth could be obtained by doubling the concentration of egg yolk or by adding 0.5 per cent. of Wilson liver concentrate powder (Wilson Laboratories Chicago) C M Wanyon

STOLL Alice M. WARD P A & MATHIESON D R The Effect of Ultraviolet Radiation on Cysts of *Entamoeba histolytica* *Science* 1945 May 4 463-4

The radiation employed was from two types of lamp emitting energy of wavelength 2,537 Å. Cysts were suspended in distilled water in concentration of 30,000 per litre. After irradiation the suspensions were sedimented, and the deposit was planted into suitable media. It was found that with an exposure of ten minutes all cysts were destroyed. When heavier suspensions were exposed for shorter intervals only a portion of the cysts were destroyed. In these cases however the resulting culture amoebae were abnormally sluggish suggesting a sub-lethal effect of ultra violet radiation. C M Wanyon

DEL SEL, M. Absceso amibiano de base del pulmon derecho con pleuresia reaccional de gran cavidad vaciada esta por vomica. [Amoebic Abscess of the Base of the Lung] *Rev Asoc Med Argentina* 1945 July 30 v 59 No 562, 849-51 6 figs.

WAR OFFICE. ARMY MED DEPT BULL. No 51 1945 Sept. 2-3 Treatment of Amoebic Dysentery

Treatment of amoebic dysentery should begin as soon as possible after the diagnosis has been made and the patient has been got under conditions that allow his treatment to be satisfactorily carried out. According to the stage of the disease when it comes under treatment one or other of the three courses A B or C is recommended.

Course A (for acute cases with vegetative *E. histolytica* in the stools)—Emetine hydrochloride gram 1 daily by hypodermic injection for 4 to 6 days is usually enough to control the acute symptoms. Without any interval this

should be followed by the oral administration of Emetine Bismuth-Iodide (E.B.I.) in doses of grains 3 daily for 12 consecutive days. Great care should be taken to ensure that the E.B.I. is given in suitable form. Inspection of the stools should be made regularly to see that the capsules are not being passed undissolved. It may be emphasized that E.B.I. must blacken the stools if the capsules are disintegrating properly. Along with the E.B.I. a chinlofon retention-enema, preceded by an alkaline wash-out, should be given daily. The daily enema of chinlofon (quinoceryl yatrien quinosolphan) should at first be 200 c.cm. of a 2½ per cent. solution but the quantity and strength may with advantage be increased if the enema is well tolerated. The important point is that the enema should be retained by the patient for at least six hours and to ensure successful retention he should be kept at rest during this period.

When this stage of the treatment has been completed, one 0.25 gramme tablet of stovarsol or carbarsone should be given twice daily for 12 days. If diodoquin is available it should be used in this after-treatment instead of stovarsol or carbarsone. 3 tablets, each containing grains 3.2 (0.2 gramme) should be given three times a day for 20 days. During this stage the patient may be allowed to get up and begin his convalescence.

"Amoebic and bacillary dysentery often occur together and this complication may be suspected on clinical grounds from the presence of a particularly acute attack. In this circumstance it is of benefit to give sulphaguanidine or sulphasuxidine (succinyl sulphathiazole) 5 grammes 4-hourly along with the emetine injections.

"*Course B (for patients who are passing cysts but not vegetative forms of E. histolytica and who present neither acute dysenteric symptoms nor indications of hepatitis)*—The hypodermic injections of emetine are omitted. Treatment by oral E.B.I. with retention-enemas and the follow-up course of stovarsol, carbarsone, or diodoquin, is begun at once and carried through as in course A.

"*Course C (for intractable cases that resist ordinary treatment)*—Cases of amoebic dysentery that resist course A will usually respond to it after a preliminary course of penicillin and sulphasuxidine has eliminated secondary pyogenic organisms which have become established in the diseased bowel wall. Best results have been secured by giving 100,000 units of penicillin intramuscularly as an initial dose and continuing treatment with 33,000 units every 3 hours until 2 million units have been given. The sulphasuxidine is given concurrently in 5 gramme doses every 4 hours until 80 grammes have been given. If necessary sulphadiazine, sulphathiazole, or sulphaguanidine may be used in appropriate dosage as substitutes for sulphasuxidine.

"It should be realised that there are exceptional cases which resist these lines of treatment. The best plan in this event is to allow a suitable interval and then repeat the whole course.

"*Criteria of cure*—Amoebic dysentery is notoriously liable to relapse. Stools should be examined microscopically at regular intervals during treatment and macroscopically on six consecutive days at least 2 weeks after all treatment has been completed. This interval between the end of treatment and the beginning of the laboratory clearance tests is important. Sigmoidoscopic examination for test of cure should likewise be deferred until the same time.

General considerations—Correctly given drug-therapy should be supported by a cheerful ward-atmosphere and good nourishing food. Milk may be given from the first and followed as soon as possible by a nutritious low-residue diet of high caloric value. Vitamins in some form—multivite tablets, for example—may sometimes have to be added.

WAR OFFICE ARMY MED DEPT BULL. NO 51 1945 Sept 3-4 Treatment of Hepatic Amoebiasis

Only the vegetative stages of *Entamoeba histolytica* are ever found in a liver abscess cysts have never been discovered there. This is fortunate for treatment because the vegetative stage is far more amenable to emetine injections than the cysts. It is largely for this reason that most cases of hepatic amoebiasis even if there is early pus formation will respond to a relatively short course of emetine injections. It must not be forgotten however that the underlying intestinal condition will almost certainly need longer and perhaps repeated courses of combined treatment.

Emetine hydrochloride grain 1 should be given daily by injection for 9-12 days. If the symptoms are not relieved and pus is suspected the liver should be needled. A 20 c cm. syringe with wide-bore needle $3\frac{1}{2}$ to 4 inches long is the best instrument for this purpose. Unless there is some special indication such as a point of local tenderness or a local area of oedema the puncture is best made at the site of election—that is the 8th to 10th inter space in the mid-axillary line. Premedication with morphine and hyoscine or some other sedative is usually advisable. Local anaesthesia is employed for the needling. If pus is found on exploration an effort is made to drain the abscess cavity with a Potain's or other closed aspirator. Several such aspirations may be necessary at intervals of a week or more. In some cases repeated aspirations fail to effect a cure and the patient continues to go downhill. Use must then be made of some form of closed suction drainage or as some surgeons prefer open drainage with removal of one or more rib sections. It must be remembered that there may be more than one abscess. It is worth noting that after pus has been evacuated from a large abscess shrinkage of adjacent liver tissue may greatly raise the cavity. Later aspirations must then be done at a higher level or with open drainage a new and higher incision may become necessary.

SILVERMAN D N & LESLIE A. Toxic Effects of Diiodoquin. *J Amer Med Ass* 1945 Aug 11 v 128 No 15 1080-81

Diiodoquin (5 7-diiodo-8-hydroxyquinoline) since its introduction for the treatment of amoebiasis has been regarded as non toxic even when taken in large doses for a long period. Many writers have noted this. The present record is therefore interesting and important in showing that the drug cannot always be taken with impunity. The dose originally recommended was one or two tablets each of 0.2 gm. (3.2 grains) three times daily but it was found that larger doses 3-4 tablets thrice daily gave better results and did not cause toxic effects.

The present authors put on record three cases. Two were given four tablets three times daily the first for 19 days, the second for 8 days (with emetine injections for five and four days respectively). Both developed a furunculosis necessitating incisions and drainage. The third patient was a woman of 51 years she received the same daily dose of 12 tablets for 23 days. She then complained of sore throat and chilliness and a blotchy erythema appeared involving the whole body. This cleared up in about a week. Later examination of the stools of these patients failed to show amoebae in the last case as long as one year after treatment.

H Harold Scott

PAYNE A. M M COGHILL, N F Amoebic Dysentery [Correspondence.] *Lancet* 1945 Sept. 8 319

i In a previous paper [this *Bulletin* 1945 v 42, 381] Payne reported that sulphapyridine and sulphaguanidine allayed symptoms in chronic amoebic

dysentery in India without affecting the amoebae in this country [Britain] he has recently treated six cases of chronic amoebic dysentery and four cases of ulcerative colitis with succinyl sulphathiazole [“sulfasuvidine”] and penicillin as advocated by HARGREAVES [this *Bulletin* 1945 v 42 895].

In the dysentery cases the results confirmed Hargreaves' claims and two of the ulcerative colitis cases improved greatly and rapidly but the author is not confident that they were cured. The other two cases showed only slight improvement.

Both in India and in this country the medical officer should satisfy himself that hospital orderlies give the enemata properly as they are sometimes careless and inefficient.

u During the last two years Coghill has treated 70 acute and chronic cases of amoebic dysentery in the Middle East with 12 daily injections of 1 grain of emetine together with sulphonamides by the mouth. The sulphonamides were usually sulphaguanidine (3.5 gm. four hourly for 10 days—total 220 gm.) together with sulphathiazole (0.5 gm. five times a day for 7 days). The results are not given being still incomplete but the author supports the opinion of Hargreaves and suggests further that bactericidal drugs should be given concurrently with emetine not only in chronic amoebic dysentery but in all forms of the disease. J. F. Corson

D'ARCANGELO D. Contributo allo studio della Lamblasi intestinale in Addis Abeba. Nota \ 1 [*Giardia* Infection in Addis Abeba.] *Boll Soc Ital di Med e Igiene Trop* (Sex. Entrea) 1944 v 4 No 3 463-74. English summary (4 lines).

— Contributo allo studio della Lamblasi intestinale in Addis Abeba. Nota \ 2 *Ibid* 475-85 [27 refs.] English summary.

The author having had under observation 71 cases of *Giardia* infection in Addis Abeba publishes his results together with a review of a selection of the literature dealing with this subject. He finds that infection always results in a duodenitis, associated with colitis in 30-40 per cent of the cases. In some cases especially in children, symptoms of dysentery occur. Atebrin is regarded as a specific remedy for the infection but it is stated that this drug acts only on the vegetative forms and not on the cysts for which it must be given per rectum. [Such a statement suggests that the author does not realize that if all vegetative forms are destroyed cysts are no longer produced. It is no more necessary to destroy cysts of *Giardia* in the intestine than cysts of *Entamoeba histolytica* or eggs of intestinal helminths in order to bring about a cure.] C. M. Wemyss

RELAPSING FEVER AND OTHER SPIROCHAETOSSES

SWYER G. I. M. Rel Btts Fever due to Cat Btts. Satisfactory Response to Penicillin after Failure of Arsphenotherapy. *Brit Med J* 1945 Sept 22 396-7 1 chart.

The clinical symptoms are described in detail and are fairly typical of the disease but the most aberrant and striking feature of the case was a severe and recurrent myositis with pain and swelling in various muscles, which rapidly subsided after treatment with neoarsphenamine but reappeared several times until finally cured by penicillin. The patient became ill about three weeks after being bitten and was admitted to hospital a week later.

Direct blood examination during a febrile attack on the 16th day was negative, but during the next febrile period blood was inoculated into mice which showed spirilla a week later

Neocarsphenamine (0.45 gm) was given intravenously and the next day the temperature fell to normal but 15 days later there was a relapse and a second injection (0.6 gm) was given followed by a third dose eight days later. The patient was then discharged but three weeks later there was a return of symptoms and he was readmitted to hospital and given four more injections of neocarsphenamine. After about six weeks the symptoms had completely disappeared and the patient himself claimed to be feeling quite well.

Three weeks later he was readmitted a third time five to six months after the original infection and on this occasion was treated with penicillin 15 000 Oxford units three-hourly by intramuscular injection for five days. The temperature was 100.8°F on admission rose to 104°F the following day but within 24 hours it had fallen to normal and remained so within four days the patient was feeling perfectly well.

Finally the author comments on the unsatisfactory name rat bite fever which is used for two different infections and suggests the term *spirillosis* as being less objectionable. E HANDLE

THOMPSON R B A Case of Rat bite Fever [Memoranda] *Brit Med J* 1945 Sept. 22, 388 1 fig

YAWS

DA CUNHA A M LEÃO A E A GUIMARÃES F N & CARDOSO H T Ensaio terapêuticos com penicilina. I Bouba (Framboesia Plan. Yaws) Nota prévia. [The Treatment of Yaws with Penicillin.] *Mem Inst Oswaldo Cruz* 1944 Apr v 40 No 2 185-200 4 pls. English summary

The first results of treatment of yaws by Penicillin are here reported

In seven patients a complete disappearance of the external lesions was obtained between the 12th and the 44th day of treatment and serological reactions were negative on the 60th day in all cases. The observations of the patients will be continued for six months under immunologic controls each 8 days

The treatment has been performed, using a mean dosage of 200 Oxford units each 4 or 6 hours. The total amount of units per subject has varied from 9 600 to 52 000

No toxic phenomena due to the drug have been observed in spite of the frequency and the high number of injections

DA CUNHA A M GUIMARÃES F N LEÃO A E A & CARDOSO H T Ensaio terapêuticos com penicilina. III Bouba (Framboesia plan yaws) Penicilina de procedência americana empregada em doses baixas também cura aparentemente esta enfermidade. [The Treatment of Yaws with Penicillin.] *Mem Inst Oswaldo Cruz* 1944 Oct v 41 No 2 247-55 5 figs English summary

Five patients of yaws were treated with American penicillin (Squibb Winthrop and Lilly) in small doses. The treatment has been performed

using 200 Oxford units each 4 hours. The total amount of units per subject, has varied from 24,000 to 54,000.

A complete disappearance of the external lesions was obtained between the 12th and the 25th day of treatment.

LEPROSY

MURR E. Future Programme of B.E.L.R.A. A Progressive Plan for the Control of Leprosy in the British Colonies. *Leprosy Review* 1945 Aug v 16 No 1 14-21

During the first twenty-one years since the foundation of the British Empire Leprosy Relief Association (a short history of whose work has recently been published in pamphlet form by B.E.L.R.A.) the Association has been mainly engaged in the pioneer work of demonstrating the value of the improved treatment of leprosy through the injection of soluble preparations of chaulmoogra oils, and in epidemiological studies to determine the simplest methods of finding and treating the early stages of the disease, which are alone amenable in large numbers to that treatment. The history above referred to demonstrates the success of these modern methods of control in Nigeria, British Gambia, Ceylon, India, etc. and opens the way to their more general adoption by the Governments of the many leprosy-infected areas of the British Empire. A new situation has arisen since the Colonial Development and Welfare Scheme recognized the value of the anti-leprosy work already accomplished and provided grants towards extending the work. The most noteworthy of these is the sanction of an expenditure during the next five years of £258,000 to cover the capital and recurrent costs of a new leprosy department of the Nigerian Government to take over the doctors, nurses and lay workers of the very successful leprosy agricultural colonies which have been largely organized and financed hitherto by B.E.L.R.A. and various missionary bodies. This will free £3,500 a year and thus enable the Association to extend its work in other Colonies, especially those of severely infected African tropical countries, and also to extend research work with a view to carrying out prolonged and carefully controlled tests of sulphonamide and other promising drugs with a view to establishing a more effective treatment of the difficult infective lepromatous types of leprosy which if successful will hasten very greatly the reduction and eventual eradication of the disease from a great part of our empire.

After pointing out the great opportunities thus opened out of still more effective work for B.E.L.R.A. as soon as doctors and others become available for employment under the Association to finance whom a special appeal is being made this year Dr Murr gives in this paper a brief survey of the most urgent requirements of the following British Colonies and Territories. Nigeria presents the most serious Empire problem outside India, on which B.E.L.R.A. has especially concentrated its efforts in recent years. A number of additional medical and lay staff will be required to extend the work; they can best be recruited and trained by B.E.L.R.A. The Equatorial province of the Anglo-Egyptian Sudan presents another large problem, where work by the Government and by the C.M.S. is already in progress but requires material extension

In East Africa much pioneer work has been done by medical missionaries with B.E.L.R.A. help but only the surface of the problem has been touched plans for greatly extending the work only await the necessary staff and funds. In West Africa very little has yet been done in the Gold Coast Sierra Leone and the Gambia. In the West Indies the Colonial Development Fund is now giving assistance but more workers are required and the same remark applies to several smaller infected areas. There is thus ample scope for further work by B.E.L.R.A.

L. Rogers

SHAMLA RAO A. *Leprosy Surveys in Hyderabad Deccan. Leprosy in India* 1945 Apr v 17 No 2 64-8 1 map

This is the third and concluding report of a leprosy survey of the Hyderabad State in the Deccan and the results of the whole work are illustrated by a map showing the incidence of the disease in each of the 15 districts. From this and the tables of data it appears that the east central districts have the highest rates (0.5 to 1.0 per cent) and western districts the lowest (0.1 to 0.3 per cent). The north and south-eastern districts show the intermediate rates of 0.31 to 0.49 per cent. No explanation is given of these differences. The rates found by complete surveys of the population of the villages within a five mile radius of leprosy clinics at hospitals or dispensaries were from 10 to 40 times higher than the figures of the censuses made in these areas in 1931. This is due to the number of early cases found by the survey parties. Males numbered three times as many as the females found by the surveys but owing to the purdah system and the want of a female doctor in the survey party this ratio is not a true picture of the actual conditions. The percentage of lepromatous cases showed the high figures of 31 to 43 per cent of the total cases. The proportion of children below the age of fifteen was above 10 per cent. in only one of the three districts now reported on.

L. Rogers

LEPROSY IN INDIA. 1945 July v 17 No 3 88-100 1 graph. Annual Report of the Indian Council of the B.E.L.R.A. for the Year 1944

Much of the work referred to in this report has already been published and dealt with in previous abstracts, but the following additional points are worthy of mention. The work has been maintained in spite of war difficulties. Many army medical men have been trained in the diagnosis and treatment of leprosy and during the year 177 patients have been referred to the Leprosy Department for diagnosis. In 126 of these the presence of leprosy was confirmed. Research work included long term study of selected cases to correlate clinical histological and immunological findings and intensive leprosy surveys in selected areas of India to study racial climatic and other factors influencing the incidence of the disease. It was thus found that a comparatively high lepromatous rate may be accompanied by low gross incidence and a low child rate in areas where some sort of isolation is practised and vice versa. This indicates a reduction in new cases where isolation is attempted and where the people are apprehensive regarding the spread of leprosy. Teaching publishing and propaganda work have been continued. The financial position of the association continues to be satisfactory. Immunological studies have been extended to trials of the reactions produced by non lepromatous acid fast bacilli but such preparations have not yet proved of value for the lepromin test which would be simplified if they could be used because they are easily cultivated. Sulphapyridine has not proved to be of value in the treatment of rat leprosy.

L. Rogers

DE SOUZA ARAUJO H. C. Infecção de ratos brancos com suco ganglionar de leproso seguida do isolamento dum bacilo ácido-álcool resistente de orgãos do mundo em meio de Loewenstein. Nota prévia. [Infection of White Rats with Gland Juices from a Leper. Isolation of an Acid-fast Bacillus from the Tissues of the Rat.] *Mem Inst Oswaldo Cruz*. 1941 v 38 No 3 379-85 15 figs. on 4 pls

A man of 26 years presenting extensive leprosy lesions on face, ears, trunk and limbs and enlarged cervical and inguinal glands. Pus from one of the inguinal glands was found to be rich in Hansen's bacilli and a white rat was inoculated with it, subcutaneously in the axilla, as recommended by Marchoux. Five months later the rat was killed: the axillary and inguinal glands were enlarged and contained bacilli morphologically resembling Hansen's organism. The patient's glands were again punctured and one cc. of pus obtained emulsified in 3 cc. saline and injected, 1 cc. into each of three white rats. Fifteen months later one rat died and showed bacilliferous lesions in the spleen. Two months after this the second rat died and its glands and viscera were rich in acid-fast bacilli, and tubes of Löwenstein's medium were inoculated and a culture obtained. Eighteen months and one week after the inoculation the third rat died, with areas of alopecia and marked glandular enlargement with many bacteria. Sections of the organs did not reveal any of these bacteria. More tubes of the medium were sown with the gland juice and fifteen days later there was a yellow-coloured growth consisting of acid and alcohol-fast organisms, singly and in masses: see the following abstract.]

H Harold Scott

DE SOUZA ARAUJO H. C. Cultura cromogénica dum bacilo ácido-álcool resistente isolado de pus de lesão fechada de lepra humana. [Chromogenic Growth of an Acid- and Alcohol-fast Organism obtained from a Human Leprosy Lesion.] *Mem Inst Oswaldo Cruz*: 1942, v 37 No. 1 29-34 2 pls. (1 coloured) English summary p. 32

A boy of 7 years, both of whose parents were lepers showed numerous leprosy manifestations in various parts of his body. One of these which fluctuated was opened with a galvano-cautery and pus was evacuated in which Hansen's bacilli were present in large numbers and no other organism seen. Inoculation was made with this in tubes of Löwenstein's medium and also into guinea-pigs and white rats. In ten weeks three of these tubes (and also two of another lot which had been sown less than 3 weeks before) contained an abundant growth consisting of masses of acid- and alcohol-fast organisms and subcultures were made. Coccoid forms predominated, like *Mycobacterium fortuitum* described by MARCHOUX in 1923: others were like those of KZENKOWSKY and DUVAL on glycerin agar but more of an orange than a golden yellow. Further subcultures were made on glycerin potato glycerin broth and glycerin agar (all with 5 per cent. glycerin) and the yellow growths were obtained with all of them. The early growth was mostly of the coccoid forms later bacillary when transferred to the glycerin media. They were always acid and alcohol-fast.

In an addendum the author describes the results of animal inoculation and further subcultures of the organism. Abscesses in the peritoneum axilla and elsewhere revealed the same organism, but smears from the internal viscera were negative. Portions of the tissues have been sent to Dr Torres and to other laboratories for examination and experimental work. A coloured plate shows well the growth and its characters.

H Harold Scott

DE SOUZA ARAUJO H C & MIRANDA R. N. Poderá o carrapato transmitir a lepra? Mais quatro amostras de culturas de bacilos ácido-alcool resistentes obtidas de carrapatos (2 de *Amblyomma cajennense* e 2 de *Boophilus microplus*) infectados em leprosos do Paraná. 3a Nota. [Is the Tick a Transmitter of Leprosy?] *Mem Inst Oswaldo Cru* 1942 v 37 No 3 391-425 23 figs. 19 refs.] English summary

The subtitle of this article—the material on which it is based—is four more specimens of culture of acid and alcohol fast organisms obtained from *Amblyomma cajennense* and *Boophilus microplus* infected from lepers in Paraná.

The account is very detailed but the upshot of it is that Dr Miranda who is head of the São Roque leprosarium allowed a number of ticks to feed on lepers and then sent the insects to Professor de Souza Araujo. On examining them the latter found that *Amblyomma cajennense* and *Boophilus microplus* could infect themselves from the lepers and that the organisms thus taken in would grow on Löwenstein's medium. A study of these cultures is now proceeding and animal inoculations into white rats are to be carried out. These ticks it was observed can pass from one host to another and continue their feeding so that organisms acquired from one host may be transmitted directly to a second.

H Harold Scott

DE SOUZA ARAUJO H C Infecção espontânea e experimental de Hematófagos (Ixodídeos Triatomídeos Culicídeos Hirudíneos Pediculídeos e Cimicídeos) em leprosos. Possibilidade de serem eles vectores ou transmissores da lepra. [Natural and Experimental Infection of Blood-sucking Insects and Leeches from Lepers.] *Mem Inst Oswaldo Cru.* 1943 June v 38 No 3 447-84 21 figs. [30 refs.] English summary

The author quotes from the reports of other investigators and then proceeds to relate the results of his own experimental work in testing whether the insects in question become infected after being allowed to feed on lepers. Details are given of each set of experiments and for general information these may be summarized as follows —

Ticks—*Amblyomma cajennense* and *Boophilus microplus* caught feeding on lepers were found to contain bacilli acid and alcohol fast. Hansen's organism but growth of them was not obtained. Only female ticks were found thus infected.

Triatoma—*T. infestans* and *Panstrongylus megistus* [*T. megista*] were found naturally infected. Experiments were carried out with these and with *Rhodnius prolixus* and other Reduviids and it was found that the larvae of *T. infestans* do not insert the proboscis deeply into the skin, whereas the nymph and adult penetrate more deeply and infect themselves. Some writers have affirmed that bacillaemia occurs in lepers only at the time when there is fever but this appears to be erroneous.

Culicidae—*Psorophora ciliata* *P. varipes* *P. ferox* and *Aedes crinitus* were found to have ingested many bacilli after feeding on a leper.

Leeches—Diametrically opposing opinions have been stated as to the infectivity of water leeches. Some have stated that after sucking the blood of lepers no bacilli can be found, others that they are to be seen every time. VAN BREUSEGHEM in 1937 [this *Bulletin* 1937 v 34 905] examined 165 specimens taken from Lake Egoba in the Congo much frequented by lepers and found the organism in three of them very many in one. The author convinced himself that leeches do ingest the organisms and excrete them in their faeces.

Cimicidæ—GOODRICE and others have reported finding these bacilli in *Cimex lectularius* which had fed on lepers but the author did not find any positive among specimens collected in the beds of lepers and sent to him for examination
H Harold Scott

DE SOUZA ARATJO, H. C. Verificação em condições naturais da infecção de mais três Hematófagos (*Anopheles Flebotomos e Simuliídeos*) em lepro-sos. Natural Infection of Three more Blood-sucking Insects from Lepers. *Mem. Inst. Oswaldo Cruz.* 1943 Oct v 39 No 2, 167-76 14 figs. English summary

Ten lepers, all L3 were selected and insects which bit them were captured and examined. The author had previously demonstrated infection by acid- and alcohol-fast bacilli in the body louse and in the nymph of the tick *Amblyomma cayennense* and these findings he was able to confirm, but he also found that two species of *Anopheles*—*A. allstonsi* and *A. tarsimaculatus*—were heavily infected, that *Phlebotomus intermedius* showed the bacilli in both the proboscis and the stomach, they were present also in smears made from two specimens of *Simulium* (*S. portinax*?)
H Harold Scott,

DE SOUZA-ARATJO H. C. Culturas de bacilos ácido-álcool resistentes isolados de hematófagos infectados em lepro-sos. Evidências de se tratar do bacilo de Hansen. Culture of Acid- and Alcohol-fast Organisms from Blood-sucking Insects which have fed on Lepers. Evidence that these are Cultures of Hansen's Bacillus. *Mem. Inst. Oswaldo Cruz.* 1944 Feb. v 40 No 1 9-31 20 coloured figs. on 1 pl. & 40 text figs. English summary

The author has made a series of cultures primarily from human leprosy lesions and secondarily from the blood-sucking insects which have fed on leper patients or from animals (guinea-pigs and white rats) inoculated with the primary cultures. He has now succeeded in obtaining 7 cultures. (1) The primary one direct from a leper (he obtained subcultures from this by inoculation of guinea-pigs and white rats). (2) Two isolated from *Amblyomma cayennense* which had been allowed to feed on lepers—two from *Boophilus microplus* similarly obtained. (3) Two from *Triatomídeos*, *T. infestans* and *Panstrongylus megistus*. The characters of the growth have already been described (above) and they are well shown in a coloured plate of 20 figures. Penicillin, which acts so potently on some Gram-positive bacteria, has no effect on this organism.
H Harold Scott

DE SOUZA-ARATJO H. C. Verificação da infecção de moscas da família *Tachinídeæ* pela *Empusa* Cohn 1855. Essas moscas, sugando úlceras lepro-sicas se infectaram com o bacilo de Hansen. Infection of *Tachinídeæ* by *Empusa* and Hansen's Bacillus. *Mem. Inst. Oswaldo Cruz.* 1944 Aug., v 41 No. 1 200-208 3 figs. English summary (8 lines)

On an ulcerous lesion of the left external malleolus of a leper a large number of flies were feeding. Some were captured and were diagnosed as *Tachinídeæ*—they were too few for the species to be determined, but it was thought that they were of several species. They were all dead by the following day and in their intestines were acid- and alcohol-fast bacteria mixed with the fungus *Empusa*. Cultures of the bacteria on Löwenstein's medium were attempted, but time was allowed to elapse and they were overlooked. The work is to be taken up again.
H Harold Scott

DE SOUZA ARAUJO H C MARIANO J & DE OLIVEIRA CASTRO G M
Tentativas de transmissão da lepra ao homem por meio de Triatomídeos
infectados em doentes lepromatosos (Nota prévia) [Attempts to transmit
Leprosy to Man by Triatomidae which had fed on Lepers.] *Mem Inst*
Oswaldo Cruz 1944 Dec v 41 No 3 495-505 4 figs English summary

Professor de Souza Araujo has already demonstrated [above] that
Triatomidae *T. infestans* and *Panstrongylus megistus* after feeding on a leper
harboured bacteria which were acid and alcohol-fast and could be grown on
Löwenstein's medium. With his fellow workers he has now studied whether
these insects thus infected can later infect human beings. To test this they
bred *T. infestans* and *P. megistus* in the laboratory till they were sufficiently
developed to bite man when they were allowed to feed on burned-out leprosy
patients. Five months later a few acid fast bacilli could be seen in the lymph
lying under the site of the bite—not a very satisfactory result so far but the
patients are being kept under observation for further study. [Not a very
satisfying paper if the disease does develop it may be looked upon as a
lighting up of a condition believed to be burned-out and if it does not the
question arises whether a burned-out case is re-infectible.] *H Harold Scott*

DE OLIVEIRA CASTRO G M & MARIANO J Transporte e inoculação de bacilos
da lepra pelos mosquitos [Mosquitoes and Leprosy Transmission.] *Mem*
Inst Oswaldo Cruz 1944 Dec. v 41 No 3 511-24 3 figs & 2 coloured pls

It is known that after mosquitoes have bitten a leper the bacteria can be
demonstrated in the alimentary canal of the insect but whether the mosquito
can inoculate a healthy subject is not known

Volunteers having allowed themselves to be bitten by such mosquitoes were
examined after intervals varying from 14 to 31 days. Lymph was withdrawn
from the site of the bite. Bacteria were not found but sections of the skin
revealed a perivascular infiltration of the superficial plexuses of the skin no
apparent change in the epidermis, but acid and alcohol fast bacteria were seen
in the connective tissue spaces not in the cytoplasm as is usual in leprosy.
Whether the mosquitoes really infect at the time of biting or whether the
negative burned-out cases (on whom these tests were tried) are not really
abacilliferous but paucibacilliferous [*i.e.* still harbour a few organisms]
or thirdly whether the bite has set up a *locus minoris resistentiae* with con-
sequent multiplication of a few local pre-existing organisms which of these
three hypotheses is the correct interpretation of the findings remains to be
proved *H Harold Scott*

IBARRA PEREZ R. & GONZALEZ PRENDES M A Síntomas iniciales de la lepra.
[Earliest Symptoms of Leprosy] *Rev Sifilografía Leprologia y Dermatolo-*
gía Marianao Cuba. 1945 June v 2 No 2 108-11

Between the time of inoculation by Hansen's organism and the appearance
of symptoms there is usually a long silent period. In children separated from
their parents the interval ranges up to five years. Though the number of
bacilli in a lesion is large its presence may pass unperceived. Reports of the
incubation period between inoculation and appearance of symptoms as for
example infection of a wound a surgical operation by use of a leper's razor
and so on are not conclusive because the subjects were all living with lepers
or in contact with them and might have been infected earlier or at any time.

The authors have noted the initial lesions, that is the first signs observed by
patients in 760 cases and in a list they gave the numbers and percentages of
the first symptoms. Erythematous maculae were given as the first seen by

139 (18.3 per cent.) achromic maculae in 104 (13.7) dark macular in 45 (6) + macular lesions in 288 or 37.9 per cent. areas of anaesthesia in 71 (9.34) infiltration of the ears in 68 (8.7) systemic disturbance with fever in 49 (6.44) rhinitis in 33 (4.33). These are the chief and the great majority were first observed in uncovered parts face, neck, arms chest and feet. It is noticed that rhinitis comes a good way down the list and the authors are of opinion that the nose is not the portal of entry but the portal of exit. After a period of time, the bacillus, having gained entry finds its way to the lymph or blood capillaries. If the former the development is slow if the latter dissemination is more rapid and widespread, and symptoms such as general malaise headache fever and rheumatic pains are observed. *H Harold Scott*

DE SOUZA ARAUJO H C A lepra tuberculóide, ou melhor a lesão tuberculóide na lepra, representa uma fase de transição desta dermatose e não uma forma clínica autônoma. Novos achados bacterioscópicos na linfa subcutânea de leprosos. [Tuberculous Lesions not a Distinct Form of Leprosy] *Mem. Inst. Oswaldo Cruz.* 1943 Aug. v 39 No 1 77-86 18 figs. [12 refs.] English summary.

The author brings evidence to show that the division of leprosy into lepromatous tuberculous and macular types is an artificial one and rests on no sound basis. In his view all cases are mixed, those regarded as cutaneous have also the nerves to the part affected. Using the Lleras technique of examining the cutaneous lymph [see this *Bulletin* 1944 v 41 220] in so-called tuberculous cases he found small granules and coccobacillary forms of the organism, acid and alcohol fast. Relapses in burned-out cases are due it is said, to development of these forms of the bacillus. The article contains a series of excellent photographs showing the "tuberculous form" of leprosy. *H Harold Scott*

GONZÁLES URRUTIA, J Alopecia leprosa en México [Leprotic Alopecia in Mexico.] *Rev. S. filografía, Leprología y Dermatología.* Mariano Cuba. 1945 June, v 2, No 2, 73-100 20 figs.

DE SOUZA ARAUJO H C Preparo de antígenos (Leprolinas Souza Araujo) de culturas de bacilos ácido-alcool resistentes isolados de leprosos. Seu emprego intradérmico comparativamente com o da lepromina, e subcutâneo ou intravenoso como tentativa terapêutica. [Preparation of Souza Araujo Leprolins. Cultures of Acid- and Alcohol-fast Organisms obtained from Lepers.] *Mem. Inst. Oswaldo Cruz.* 1943 Dec. v 39 No 3 349-55 4 figs. English summary.

The technique for preparing the antigens is to extirpate a florid leproma rich in Hansen's bacilli, emulsify it and homogenize it by placing it in an electric shaker for 10 days and nights. Then add liquid phenol to 0.5 per cent. of the volume and, after testing it for sterility, add 0.5 per cent. phenol to 10 per cent. of the volume. It is then put up in ampoules. The skin reactions to these are the same as those with lepromin. These antigens are being tested as to their value (a) in diagnosis and (b) in treatment, and results will be promulgated later. The author kindly offers to place his products—there are five of them—at the disposal of any leprologist who wishes to test them. *H Harold Scott.*

MARIANO J Resultados do emprego das leprolinas "Souza Araujo" comparativamente com o da lepromina. [Comparison of Leprolins "Souza Araujo" with Lepromin (as regards Intradermal Tests)] *Mem. Inst. Oswaldo Cruz.* 1944 Feb., v 40, No. 1 101-19 1 fig.

Five leprolins were obtained: one from a leper, one from a guinea pig inoculated with the primary leper culture, two from cultures from *Amblyomma*

cajennense and one from *Boophilus microplus*. These were inoculated in amounts of 0.2 cc. and compared with a similar inoculation of lepromin. The tests were carried out on 10 groups of lepers namely: L1 (8 cases) N1 (7) N2 (3) N3 (6) L1N1 (11) L2N2 (3) L1N2 (14) L2N1 (16) L3N1 (19) L3N2 (4). Protocols show the results of four consecutive weekly readings in each case. For purposes of this abstract the readings (which total more than 2,000) must be grouped. In the L1 cases lepromin 4 (a strain from *Amblyomma cajennense*) gave reactions identical with lepromin the others gave differing readings. In group II the N1 cases again lepromin 4 gave the same as lepromin in the N2 a group of only three cases lepromin 2 (the guinea pig strain) agreed with lepromin among the N3 cases again lepromin and lepromin 2 were in harmony. In the L1N1 patients lepromin was negative in all. None of the lepromins agreed with this but Nos. 3, 4 and 5 all gave 9 negative and 2 positive. Among the three L2N2 patients lepromin agreed with lepromins 1 and 3 (the direct culture and one of the *Amblyomma* cultures) while lepromin 4 (the other *Amblyomma* culture) was negative with all three. In the L1N2 group lepromin 3 gave one positive and five negative whereas lepromin and all the other lepromins gave a negative. [Only six are referred to in the letterpress on this group although in the table 14 are given.] The L2N1 group we cannot speak of with certainty for the letterpress states that there were 24 patients in the group whereas the table gives details of 18 only. Anyway none of the lepromin results corresponded exactly with those of lepromin. In the L3N1 group of 19 lepromin was negative in all the nearest approach to this was lepromin 3 with two positive. All four of the L3N2 group were negative with lepromin while of the lepromins No. 2 was positive in two and negative in two the other four lepromins being negative in three.

In another group of three contacts lepromin was positive in all as were also lepromins 2 (guinea pig) 3 (an *Amblyomma* strain) and 5 (the *Boophilus* strain). Among another group of children in the Preventorium lepromins 2, 3, 4 and 5 gave the same total results two positive four negative as lepromin but the individual readings differed.

Bringing these results together the author in his summary states that in the nervous cases lepromin gave a positive in 13 and negative in 3 while lepromin 2 was positive in 12 and negative in 4. In lepromatous patients lepromin was positive in three negative in 72 the lepromin most nearly approximating to this was No. 3 with 16 positive and 59 negative.

To obtain a closer comparison it is thought necessary to make a fresh series of tests with graded doses of the lepromins. The author concludes that the lepromins can play a fundamental part in the prognosis of leprosy since the reactions enable evaluation to be made of the defensive powers of an individual patient.

H. Harold Scott

MIRANDA R. N. Resultados comparativos das reacções intra-dermicas com antígenos de bacilos ácido-alcool resistentes (Leprolinas Souza Araujo) e emulsão de lepromas (Lepromina) (Primeira nota) [Comparison of the Results of Intradermal Injection of 'Souza-Araujo' Leprolins and Lepromin. (First Communication)] *Mem. Inst. Oswaldo Cruz* 1944 Aug v 41 No 1 185-200 English summary

The author carried out tests similar to the above, on 20 lepers 17 males 3 females 13 lepromatous and 7 nervous or tuberculoid types, at the São Roque Colonial Hospital Paraná State Brazil. He obtained his samples of the lepromins from Professor de Souza Araujo. Readings were taken after 48 hours and at the end of each of the first 4 weeks. The results were in general in fairly close agreement with those of de Souza Araujo namely positive in

[December 1945]

the nervous negative in the lepromatous cases. As a rule no constitutional disturbance resulted from the inoculation, but many of the patients showed a scar at the site of inoculation, indicating local destruction of tissue although there was no preceding ulceration. In one the lepromatous lesions tended to become confluent after the inoculation.

H. Harold Scott

- MOV. A. M. & BASOMBAO G. Estudios de reactividad cutanea en lepra
 VII. Intradermo-
 reacciones provocadas por la lepromina y el 2-4
 dinitroclorobenceno. *Skin Reactions in Leprosy*. *Rev. Argentina*
Dermatofisiologia. 1945 June, 29 No 2 120-28 10 figs [28 refs.]
 English summary

The authors have previously reported their results with these antigens (see this Bulletin 1944 v 41 1049 and now put on record further tests using the same technique as before. The reaction is read at 48 hours (the early reaction) when, if it is positive the redness and oedema are not less than 10 mm. in diameter and at the third week (the later or delayed reaction) when there is a nodule not less than 5 mm. in diameter with or without softening or central ulceration. The nodular or late reaction begins to show itself at the end of the first week and progresses for a fortnight. It may last for 6 weeks or more and may but does not always leave a scar. Those are classed as doubtful in which the early reaction is between 5 and 10 mm. and the late 3-5 mm. in diameter.

Tests were performed on 223 persons. 71 lepers with lepromatous 90 with tuberculous leprosy. 21 non-characteristic lepers (182 lepers in all) 15 apparently healthy persons living with lepromatous cases and 28 healthy subjects having as far as was known, no contact with lepers.

In the 71 lepromatous patients the reactions were mostly negative with both antigens, early and late. The tests agreed in 69 in the early reactions and disagreed in two with the late reaction both were the same in all 71.

In the 90 tuberculous cases the reactions were positive in the majority and were concordant. With the early reaction there was agreement in 75 non-agreement in 15. With the late reaction the respective figures were 81 and 9.

In the 21 non-characteristic simple inflammatory form, 19 gave the same reactions with both antigens at the early reading two were discordant whereas Of the 15 apparently healthy subjects four were not.

Of the 15 apparently healthy subjects four were not the same reactions to both antigens. Last of the 28 healthy subjects the early reaction was concordant in all but one (dinitrochlorobenzene negative) (both lepromin positive dinitrochlorobenzene negative) the late reaction was concordant in 24 discordant in two (both lepromin positive) the late reaction was concordant in 24 discordant in two.

The histological changes set up by the intradermo-reaction to both these antigens were studied by staining biopsy specimens at the end of 24 and of 48 hours and at the 4th 8th 16th and 30th days. These are shown by a series of well-produced photomicrographs.

H. Harold Scott

DHARMENDRA & RAJAGOPALAN S. Some Aspects of Chemotherapy in Leprosy
Leprosy in India 1945 July v 17 No 3 77-84 [53 refs]

Owing to the limitations of the hydnoacarpus oil treatment of leprosy the search for a more effective treatment for advanced cases is necessary. If early control of the disease is to be obtained. Drugs of the sulphonamide group have not proved to be of much use but sulphone compounds promise better.

mycobacterial diseases such as tuberculosis and leprosy. Of these promisin has already been favourably reported on by American workers and diasone has been found to have some prohibitive effect in tuberculosis in guineapigs as has promizole they are therefore worthy of careful trial in leprosy. The high lipid content of the mycobacteria increases their resisting powers so any change in the constitution of sulphonamides which makes them lipophilic may be expected to increase their effects. Efforts already made in this direction by other workers are summarized in this article which should be read by those interested in this line of research. The Leprosy Department of the School of Tropical Medicine Calcutta hopes in due course to report on such studies.

L. Rogers

CHORINE V. Traitement des lésions oculaires de la lèpre [Treatment of the Ocular Lesions of Leprosy] *Bull Acad Méd* 1945 v 129 Nos 13 14 & 15 230-32.

This note records promising results in the treatment of the difficult eye lesions of leprosy by local injections of sulphonamides. In order to obtain the sulphonamido in solution 60 gm of acetamide and 15 gm of sulphanilamide are made up to 100 cc with distilled water. This solution diffuses slowly through the tissues when injected around a lesion of the skin and causes its gradual disappearance. In the case of eye lesions periorbital injections are made of two to four injections of 7-10 cc of the solution but owing to the severe pain they cause local anaesthesia is first induced by the use of 1 to 2 per cent of stovaine. No complications have been noted after weekly injections at different sites. Thirteen eye cases (keratitis irido-cyclitis etc.) have been treated but five are too recent to be reported on. Of the other eight cases in four vision has recovered to normal and in one after only nine injections it has improved. In the other three blindness of several months or years duration failed to respond to the treatment but pain in the eyes has been reduced. In eye cases photophobia has been cured and rapid retrogression of keratitis has been observed. Irido-cyclitis is less quickly influenced but is eventually quieted. Moreover nasal infections have been cured in all such cases. In the case of localized dermal nodules the results are also very favourable. [Further trials of this promising method of treatment will be awaited with interest.]

L. Rogers

LEPROSY REVIEW 1945 Aug v 18 No 1 4-12, 1 56 New Drugs for Trial in Leprosy

DAVEY T F Leprosy Control in Owerri Province of Nigeria *Leprosy Review* 1945 Aug v 18 No 1 21-30

This report deals with the sixth year's work of this great leprosy colony [see this *Bulletin* 1944 v 41 53 for previous report]. Of the two million inhabitants of the Owerri Province it is estimated that not far short of 75 000 suffer from leprosy yet two of the six divisions are still untouched in spite of 18,554 patients having been brought within the scope of the work. It is impossible to isolate all the infective cases but working on a clan basis with the cordial co-operation of the people themselves 27 leper villages have been built to accommodate 1,807 of the most highly infective patients and six more are waiting development. In addition 1 179 patients are living in the central settlement nearly all infective or requiring hospital treatment. Over forty out-patient clinics supply treatment to earlier cases. Repeated surveys allow newly developing cases to be discovered and treated while still in an amenable

stage. Nurses are given eighteen months training, and 130 are already at work in the clinics and villages. Over 1 100 child patients are being cared for—the majority of these are maintained by B.E.L.R.A. a child adoption scheme financed by special subscriptions given largely by British children. Physical training, boy scout activities and various social amenities are encouraged or supplied. Twenty leprosy inspectors work in different parts of the province; they include in their duties the examination of contacts of known infective leprosy cases especially children for early signs of infection. Already in the case of six clans the present progress amounts to an approximate isolation with treatment of all infectious cases together with treatment of all the earlier cases. In these areas progress and diminution in the incidence of leprosy may be expected. Thus the practicability of effecting a rapid reduction of leprosy in Nigeria with sufficient staff and funds has been demonstrated, and it is this success which has led the Nigerian Government to take over the work with a view greatly to extend its scope.

L. Rogers

SEN J. B. Purulia Naba Kushta Nibhas (Balaranpore) A New Line of Attack on the Leprosy Problem. *Leprosy in India* 1945 Apr v 17 No 2, 43-7

This is an interesting account of a trial of a new and promising method of dealing with the serious problem of the wandering begging lepers who help to spread the disease in India, though to a limited extent because many of them are of an advanced, crippled, little infective nerve type. The term Naba Kushta Nibhas means the New Leper Home. The need for its foundation was demonstrated by the popularity of the large leprosy institution at Purulia, which attracted hundreds of begging lepers from other parts of India, who could not be admitted to the older institution. It was originally intended as a night shelter but owing to the generosity of the people of Purulia, with the aid of grants from local government bodies it has been developed into a home in which the unfortunate patients are lodged and fed four miles out of the town. It was found that many of them were fairly well-to-do persons who had been driven out by their relatives and some of them have recovered part of their property and given it for the support of the new home which now contains some 300 patients.

Many of them do agricultural work to help in the feeding of the patients and others are employed on weaving or making pottery etc. Thus new hope and interest in life is provided, and the patients are regarded as guests of the town. This plan is worthy of imitation by the numerous cities of India in which the begging leper is a nuisance discreditable to those who neglect the care of their afflicted relatives. Much money has for long been expended in India in providing homes for keeping alive maimed and diseased cattle which Hindus are prohibited from putting out of their misery because cows are sacred in their eyes. The above is however the first attempt the reviewer can recall of the people of India raising funds for providing homes for their own leper outcasts—hence its importance.

L. Rogers

LINHAKES, HERMUNO Possibilidades de transmissão e vias de inoculação da lepra murina em ratos e outros animais. [Possible Routes of Transmission of Rat Leprosy in Rats and other Animals.] *Mém. Inst. Oswaldo Cruz.* 1943 June v 33, No 3 321-51 [101 refs.] English summary

In the first part of this contribution the author mentions the many possible ways by which rats may become infected with the Stéfanky organism, giving quotations from the literature dealing with the experiments connected therewith. He deals with (1) Insect transmission by *Lucilia caesar*, *Calliphora vomitoria*, *Musca domestica*, *Harmatophorus spinulosus*, *Ctenocephalus serraticipes*

Laelaps echidninus *Polyplax spinulosa* and others showing how the organism has been found in them and attempts have been made to cultivate them usually with barren results. The insects certainly contain acid fast bacilli and if the rats devour a large number of them they may become infected but this is not insect transmission in the usual and accepted sense. It would come rather under the next heading (2) Infection by the alimentary route. Rats fight and eat their dead opponents and may thus become infected. Feeding rats with rat leprosy tissue rich in bacilli is followed by widespread infection in glands liver lungs spleen and kidneys in 24 weeks onwards. (3) Cutaneous infection scratches wounds and bites are frequent among rats owing to their fighting and the organisms can easily enter thereby. (4) Congenital transmission finds no evidential support. (5) Intranasal infiltration. Some have reported finding the organism in the nasal secretion others have tried to produce the disease by experimental instillation but without result. A certain species the camondongo has shown pulmonary infection from this but the ordinary rat is less susceptible and is rarely if ever thus infected. Other methods such as intradermal intracardiac intravenous and intracerebral are of academic interest only. Genital infection occurs experimentally and the bacteria can traverse the vaginal mucous membrane and in the end produce generalized disease.

In the second part quotations from the literature tell of the successful results of inoculation into guinea-pigs rabbits camondongos *Macacus rhesus* opossums fowls and pigeons by various routes. The author ends by giving an account of his own attempts to infect fowls and pigeons. He was able to infect the former by feeding and also by intramuscular and intraperitoneal injection the latter by intramuscular or intravenous inoculation.

H Harold Scott

HELMINTHIASIS

SARMENTO A. Nota sobre um foco de bilharziose vesical em Angola. [A Focus of Vesical Schistosomiasis in Angola.] *An Inst Afric Trop* Lisbon. 1944 Dec. v 1 No 2 375-80 1 folding map

In March 1939 the author made a health survey of the Province of Bié to determine the degree of endemicity of *Schistosomiasis haematobium* there. Several foci were found the chief being Catote Chibia and Gangueles the last extending to Cuchi. A spot map indicates some of the foci. From 1836 to 1941 registered cases of this disease in Angola have numbered 1,888 1,857 1,344 1,858 and 1,792 respectively.

In the Cuchi area the author found many cases several of the patients were passing visible blood. The total numbers examined are not stated but the percentages infested (shown by macroscopical examination of the urine) were Children 60.2 adults 21.5 or both together 54.5. Figures for other parts of Africa are given for comparison. Environs of Dakar 38.8 Toma (French Guinea) 54.5 Kiné (French Guinea) 9 Liberia 93-96 Sierra Leone 13-26 Victoria Nyassa [sic? Nyanza] 50 Mombasa 83 Southern Rhodesia 50 Pretoria 31. *Bulinus* (species not stated) was found on the borders of streams and rivers Bissombo Cuchi Luassenha and Musanga. Though the disease is not often the cause of death it reduces the working capacity of many by the resultant anaemia and debility and by lowering the power of resistance to other diseases.

H Harold Scott

MAGALHÃES A. COUTINHO B. GOUVÊA, L. LUCENA D. & IGNACIO L.
Estudos sobre a Esquistosomose em Pernambuco Brasil. [Schistosomiasis in Pernambuco.] *Mem Inst Oswaldo Cruz* 1940 Jan.-June
 v 35 No. 1 205-83 15 graphs & 29 pls

This article is divided into three parts the first treats of the epidemiology of *Schistosomiasis mansoni* in Pernambuco and is mainly of local interest. Sketch maps give the situation of Pontezinha and Vitoria places in the State where the disease prevails. These maps show the water collections and general lie of the land and by varied shading the degrees of incidence. In some parts of Pontezinha this is as high as 39 per cent. and the incidence rises with age to the 16-20 years group when it reaches 37.8 per cent. the ratio of males to females affected is almost 3:2 (21.4 and 14.7 respectively). The highest age incidence in Vitoria is in the 10-15 years age-group when it reaches 56.9 per cent. the 16-20 years group has an incidence of 52.2 per cent. Here however males are proportionately less affected than females, 36.9 to 41.4 per cent. This part is embellished with 14 photographs illustrating the local terrain.

Part II is of more general importance and will be studied by all those practising in countries where this infestation is common. It is a detailed histological study of the lesions in the various organs the rectum, liver, lungs, pancreas, spleen and glands. Forty-three beautifully reproduced photomicrographs illustrate the histological changes set up. Part III gives an account of nine patients with reference particularly to the condition of the blood and the spleen. The blood changes strongly resembled those of chronic splenic anaemia. In four cases splenectomy was carried out but the results were not good on the whole. Such changes as there were tended to better regulation in the proportions of the cellular elements. One patient improved one was lost sight of, a third showed little if any change in the blood condition and died the fourth left hospital no better.

H. Harold Scott

MAGALHÃES B. F. & DIAS C. B. *Esquistosomose de Manson—Estudos*
 [Schistosomiasis mansoni (in Brazil)] *Mem Inst Oswaldo Cruz* 1944
 Dec v 41 No 3 363-446 1 map 1 coloured pl & numerous figs. [234
 refs.]

This study is divided into four chapters. The first is a short one of 4 pages of historical interest discussing the question whether rectal schistosomiasis was brought originally by slaves from Africa or was autochthonous. The authors conclude that the evidence in favour of introduction by the negroes is not strong whereas there is much to support the view that the disease existed before the time of their introduction. The snails were present it is said before slaves were being brought and VON MARTIUS has told that among the Indians (the aborigines) there was a disease characterized by a chronic hepatitis (though other organs were also affected) and often by enlargement of the spleen, haemorrhoids and diarrhoea.

The second chapter of just over 3 pages is little more than a list of Brazilian workers who have been engaged on the subject. Chapter III occupying most of the thesis (56 pages) is concerned with antimonial treatment of schistosomiasis its dangers and the fatalities associated with its use together with experimental work on 27 patients treated with it and on 7 dogs to which the drug was given in toxic doses. Photomicrographs one in colour show well the histological changes in the liver and heart. The effects on the heart form the main subject of this study. Antimony seems to act on the capillary walls leading to such a degree of dilatation that there is a diminution in the volume

of the circulating blood associated with inadequate supply by the coronary vessels to the heart itself. The work on the effects of antimony on the heart is illustrated by over 300 electrocardiographic tracings—a few words of letter press are given on each [which is well for unfortunately the tracings are so reduced in reproduction that they are illegible even with a magnifying glass].

The final chapter is a brief one of two pages devoted to consideration of whether or not there is a cardiac form of *Schistosomiasis mansoni*. There have been very few records of myocardial lesions in this disease (except presumably after antimonial treatment) and of the many cases studied and particularly among the 22 autopsies by the authors though the ova have been found in the ileum caecum rectum liver lungs ovaries testes bladder and elsewhere there is no record of their localization in the heart—it is highly improbable therefore that there is a cardiac form of the disease.

H. Harold Scott

SCHWETZ J & DARTLAELI E. Sur la faune malacologique comparative des lacs Albert, Edouard et Kivu. [The Snails of Lakes Albert, Edward, and Kivu.] *C. R. Soc. Biol.* 1945 Jan. v. 139 Nos. 1-2, 69-72.

CAIRO. MINISTRY OF PUBLIC HEALTH. MEDICAL AFFAIRS. First Annual Report. Bilharzia Snail Destruction Section 1942 [BARLOW C. H. (Expert) & ABDEL AZIZ M. (Director)] 21 pp. 3 maps (1 folding) & 5 figs (3 on 2 pls.) 1945. Bulaq. Cairo. Govt. Press.

In Fayoum Province 4 720 kilometres of irrigation canals and drains support snail populations of the bilharzia carrier *Bulinus truncatus*. These are most abundant in the branches of Bahr Yussef in the central part of the Province where the sluggish flow and muddy bottoms of the waterways provide the most favourable environment.

The system of bilharzia control initiated in 1942 is based on two main methods. (1) Mechanical clearance of small streams not exceeding 1½ metres in width by means of standardized hand nets which also serve as a measurement of snail intensity and as a guide to the progress of the control work. A coarse mesh net removes large snails, vegetation, litter and a top layer of mud after a preliminary loosening and clearance of vegetation by hoeing and manual work. This is followed up by dipping with fine mesh nets which removes small snails, egg nests, ooe and fine plant refuse. (2) Chemical treatment of larger canals with copper sulphate. Preliminary laboratory work showed that 7 parts per million of this salt acting for 48 hours was an effective killing agent but in field practice concentrations of 15-50 parts per million were required and varied according to the amount of vegetation and silt in the canals and to the length of time available for the treatment which consists simply of dragging a bag of CuSO_4 through the water at a speed calculated to give the required concentration.

In the laboratory attached to the Snail Destruction Section problems arising in the course of the field work are studied: routine analyses of water and snails are carried out and the personnel is trained. Studies on the life span and growth of *B. truncatus* and *P. boissyi* showed that *Bulinus* lived for 11 months during which time it attained an average length of 12.5 mm. *P. boissyi* lived 18 months and grew to an average diameter of 13.2 mm. It is concluded that these species do not live longer than two years.

The annual emptying of irrigation channels for a period of 40 days causes the desiccation of the snails but does not kill them. In laboratory experiments *P. boissyi* revived after 10 months desiccation in mud and *B. truncatus* after 12 months.

Self fertilization in *P. boissyi* was demonstrated in the laboratory and was successfully continued through six generations. J J C Buckley

JAKSEN G. Observações sobre o combate à Esquistosomose humana em Pernambuco no município de Catende. Índice de infestação em *Australorbis* e emprego da cal extinta e do sulfato de cobre no combate aos moluscos. [Campaign against *Schistosoma mansoni* in Catende, Pernambuco. Incidence of infestation of *Australorbis centricornis* and their Extinction by Slaked Lime and Copper Sulphate.] *Mém Inst Oswaldo Cruz*. 1943 Dec., v 39 No 3, 335-47 14 figs. English summary (10 lines)

The district in question is heavily infested examination in one part revealed an incidence of 50 per cent. harbouring *S. mansoni*. The vector is *Australorbis centricornis* which abounds in the brooks and irrigation canals where the water is more still than in the flowing streams and rivers. The inhabitants frequent these places for bathing, for washing their clothes for fishing for collecting sand and other purposes, and in parts the Panelas River for example those dwelling on the banks have no proper sanitary arrangements and discharge their excreta directly into the water.

Experiments were carried out to test the efficacy of various strengths of slaked lime and of copper sulphate for killing the snail. Boxes 10x10x4 cm. with a gauze front were placed in the water and in them a known number of the snails. The lime or copper was then added to the water and after an interval of 24 hours the boxes were opened and the proportion of snails killed was determined. One hundred per cent. fatality was found to result from the use of slaked lime in a strength of 4-5 per thousand, and the cost of this was only 25-30 centavos per kilo.

Tests with sulphate of copper showed that in a strength of 0.5 per thousand 18 per cent. of the snails were killed in 48 hours with 1.0 per thousand [by a mistake this is stated as 0.1%] 43 per cent. were killed with a strength of 2 per thousand all were killed. The copper salt is more expensive than the lime and less easily obtained. H Harold Scott

THOMAS H. M. Jr & GAGE D. P. Symptomatology of Early Schistosomiasis Japonica. *Bull U.S. Army Med Depts* 1945 Aug. v 4 No 2, 197-202.

The authors give an account of 41 cases of schistosomiasis due to *S. japonicum* contracted during the invasion of Leyte Island in 1944. The snail which serves as intermediate host in that area is *Schistosomophora hydrophora*. The date of exposure could be determined in many cases in some the infection was contracted during a single short swim in a river.

The symptomatology of the early stages of this infection is not well known. In four cases there was a feature of burning and itching sensations immediately after exposure. In others the first symptoms appeared at the end of the third or fourth week, but these might occur at any time up to the ninth week.

"On admission to hospital the chief complaints were chills fever sweats headache backache nonproductive cough abdominal discomfort and profound anorexia. Urticaria accompanied these symptoms in one-quarter of the cases and diarrhea in one fifth. Symptoms in order of frequency in 41 cases were headache 35 anorexia 30 cough 30 chills 23 abdominal cramps 18 backache 12, diarrhea 8 itching 7. Fever was present to some degree in all cases. In two cases symptoms of central nervous system origin were present. Other symptoms sometimes seen are stiffness of neck muscles, chest pain abdominal cramps and loss of weight. Symptoms and signs of acute appendicitis have been reported in other series.

Urticaria was seen in 10 cases. In two radiographs of the lungs showed small areas of infiltration. The most constant finding was enlargement of the liver (30 cases) with tenderness the spleen was enlarged in nine. The leucocyte counts were characteristic there was leucocytosis to 50 000 with eosinophilia from 15 per cent at first to as much as 90 per cent later. Schistosome eggs were first found in the stools from 6½ to 10 weeks after first exposure.

The central nervous system was apparently involved in two cases (and in one other not in this series). The patients had weakness of the arms and spasticity of the legs with increased reflexes. Sensation was normal. One patient was disorientated (he also showed signs typical of occlusion of end arteries in the toes) another was admitted in coma and died. One other patient died suddenly shortly after the ninth dose of tartar emetic he also had amebiasis but it is possible that the fatal outcome was precipitated by the drug. Fouadin and tartar emetic were the drugs used in this series. Symptoms were promptly relieved but at the time of this report it was too early to assess the final results. Treatment should be given as early as possible.

It is noted that further experience has shown that many persons may show eggs in the stools without having had more than trivial symptoms. Severe disease may develop later unless treatment is given.

Much weight should be given to a clear history of exposure. If exposure is followed in three or four weeks or less by itching, urticaria, fever, dry cough and increasing eosinophilia in the absence of other satisfactory explanation schistosomiasis may be regarded as probably present. Under these circumstances even though the diagnosis has not been proved it may be wise to initiate treatment using fouadin because of its lower toxicity. Every effort should be made however to prove the diagnosis.

Charles Wilcocks

BULL. U.S. ARMY MED. DEPT. 1945 Aug. v. 4 No. 2 178-80 The Chemotherapy of Schistosomiasis Japonica

Very little is known about the results of chemotherapy in *S. japonicum* infections. The drugs in use have been given empirically without the application of modern pharmacological techniques. The two most largely used are tartar emetic and fouadin. Neostibosan and other pentavalent antimony compounds appear to be relatively ineffectual. Antihomaline has not apparently been used and preliminary experimental work is not encouraging. Emetine cannot safely be given in effective doses.

Fouadin and tartar emetic are therefore advised. Both may be toxic and both should be injected slowly. Fouadin should be tried first. It is supplied in ampoules of a 6.4 per cent. solution of which 1.5 cc., 3.5 cc. and 5.0 cc. are injected intramuscularly on three successive days followed by 5.0 cc. on alternate days to a total of 16 doses.

Tartar emetic contains a much higher proportion of antimony. It should be made up as a 0.5 per cent. solution in 5 per cent. glucose saline (or in saline or distilled water if glucose is not available) and the first dose is 8.0 cc. given intravenously (slowly) to the recumbent patient who should remain recumbent for one hour afterwards. Subsequent doses (on alternate days) are increased by 4.0 cc. until the dose reaches 28.0 cc. The whole course comprises 15 injections.

If a second course of either of these is necessary it should not be given until two weeks after the completion of the first. The results of treatment should be checked by stool examinations for fertile eggs.

Charles Wilcocks

HUNT, A. R. Schistosomiasis in Naval Personnel. A Report of Sixteen Cases. U.S. Nav. Med. Bull. 1945 Sept. v. 45 No. 3 407-19

The infection was with *Schistosoma japonicum*.

TOREZ C. M. Alterações patológicas do apêndice vermiforme contendo Proglottos de *Taenia* sp. (Pathological Changes in the Appendix containing a Proglottis of *Taenia* sp. *Mem Inst Oswaldo Cruz* 1943 June v 38 No 3 373-84 8 figs 13 refs. English summary

CRU H. O. & DE MELLO R. P. Eliminação urinária do cloreto de sódio na anemia ancilostomílica. Urinary Excretion of Sodium Chloride in Hookworm Anaemia. *Mem Inst Oswaldo Cruz* 1944 Oct. v 41 No 2, 223-31 3 figs & 4 graphs. English summary (4 lines)

The amount of sodium chloride excreted daily in the urine was estimated in six cases of hookworm anaemia over periods of several weeks during this time the patients were given iron salts for the anaemia but no vermifuge. The haemoglobin in the blood was also measured. The results are shown in tables and charts. In three cases the amount of sodium chloride excreted daily during a control period before treatment with iron was begun was less than 8 gm. It was not correlated with the degree of anaemia, but during treatment it increased in close relation with the increase in the haemoglobin.

The authors cannot explain the diminished excretion of sodium chloride in hookworm anaemia. J. F. Corson

DESTORTES Camille. Sur *Strongyloides stercoraria* (Bavay 1876) et sur les *Strongyloides* de primates (*Strongyloides stercoralis* and the *Strongyloides* of Primates.) *Ann Parasit Humains et Comparé* 1944-1945, v 20 Nos 3-4 160-80 3 figs [Bibliography]

HODGE I. G. DEXHOFF E. J. & LINDER V. E. J. B. Early Filariasis (Bancrofti) in American Soldiers. *Am J Med Sci* 1945 Aug v 210 No 2, 207-23 3 charts 14 refs

Sixty-two cases diagnosed as filariasis bancrofti were observed they could be classified into five groups. I with genital lesions (47) II with superficial lymphangitis in the extremities (13) III with multiple lesions (16) IV with apparent involvement of the deep lymphatics (1) V with microfilariae in the blood but without symptoms (2). Cases in Group III were distributed among the other groups according to the first symptom. Notes of illustrative cases are given.

Microfilariae were found in the blood of two out of 298 soldiers, and an adult filaria was found in 1 of 8 lymph glands examined. Sections of lymphatic glands showed various degrees of inflammation with infiltration of eosinophil leucocytes.

Regarding eosinophilia as the condition when eosinophils formed 8 per cent. or more of the blood leucocytes, it was present in 18.5 per cent. of 298 soldiers exposed to filarial infection and in 5.4 per cent. of 240 soldiers not so exposed. The presence of intestinal helminths and of other causes of eosinophilia was excluded by appropriate examinations. Among the 298 who had been exposed to infection 136 showed signs of filariasis, and of these 24.2 per cent. had eosinophilia, while of the remaining 133 without signs of filariasis, 12.2 per cent. had eosinophilia. In the group of 136 soldiers with filariasis 50 had "clinical filariasis" and seven of these had eosinophilia, while of the other 86 with "minimal or doubtful filariasis" 26 had eosinophilia.

An extract of a lymphatic gland was made by digesting it for 12 hours at 37°C. with 0.6 per cent. of pepsin and 0.3 per cent. of HCl straining, standing and treating the supernatant fluid with acetone and ether until a powder was obtained. This was diluted 1:20 in normal saline containing 0.4 per

cent of phenol and was used for a skin test 0.1 cc. was injected intradermally and an erythematous weal of 0.5 cm. or more in diameter appearing within 36 hours was regarded as a positive reaction. Of 11 patients with clinical filariasis seven showed a positive reaction and all the controls (men not exposed to infection) gave a negative reaction.

The soldiers were exposed to filarial infection for 364 days and typical clinical signs were present in 41 per cent but the authors think that the rate of infection will eventually prove to have been over 50 per cent. As regards prognosis the authors think that elephantiasis is due to secondary bacterial infection superimposed on a damaged lymphatic system and that the risk of the soldiers developing it is slight. The psychosomatic effects of infection were unimportant.

Prophylaxis and treatment are briefly discussed.

J. F. Corson

FARINAUD M. E. Une médication nouvelle le violet de gentiane et les dérivés du triphénylméthane dans le traitement de l'enterose (Gentian Violet and Derivatives of Triphenylmethane in the Treatment of Enterobius Infections) *Méd Trop* Marseilles, 1944 Sept.-Oct.-Nov.-Dec. v. 4 No 4 305-11

SPRUE

CAYER D. RUFFIN J. M. & PERLZWEIG W. A. Vitamin Levels in Sprue *Amer J Med Sci* 1945 Aug. v. 210 No 2 200-207 5 charts [13 refs]

Laboratory tests recently devised for determination of the levels of various vitamins have been applied to 12 sprue patients. These were selected on the basis of steatorrhoea, glossitis, macrocytic hyperchromic anaemia, flat glucose tolerance curve and marked weight loss.

For comparison 25 patients diagnosed clinically as having mild or early deficiency of the B-complex were selected and a control group of 30 normal medical students were also studied.

All patients were hospitalized on standard diet, low in vitamins though adequate in proteins and calories. The control students were permitted to continue normal activities.

Vitamin C was measured in the Evelyn photoelectric colorimeter using Tillmans dye and the technique of MINDLIN and BUTLER (*J Biol Chem* 1938 v. 122 673). Vitamin A determinations were made by the method of HUMBLE (*J Lab & Clin Med* 1939 v. 24 1055). Those of the vitamin B-complex were determined in the urine before and after test doses of thiamin 1 mgm i.m., riboflavin after 5 mgm. orally, nicotinic acid amide, 500 mgm orally, and pyridoxine 50 mgm. orally. Thiamin was determined at first by the yeast fermentation technique of ATTON SCHULTZ and FREY (*J Biol Chem* 1938 v. 129 471) later by a modification of the thiochrome method. Riboflavin was measured by the direct fluorometric method of FERREBEE (*J Clin Investigation* 1940 v. 19 251).

The nicotinic acid load test was based on the studies of PERLZWEIG, SARETT and MARGOLIS (*J Amer Med Ass* 1942 v. 118 28). The values of F₂ determined fluorometrically paralleled closely those for total nicotinic acid excretion. Pyroxidine was determined calorimetrically by the technique of SCUDI *et al* including the form hydrolysed by treating with acid.

Vitamin A—The plasma levels of this vitamin in normal persons showed a distribution and a mean above those of the 25 vitamin-deficient subjects whilst an even lower figure was determined for sprue.

Carotene—The general distribution of values for plasma carotene was the same as that for vitamin A.

Vitamin C—Whilst there were certain individuals in each group whose plasma contained no measurable vitamin C over half the sprue patients had zero levels and the remainder were below 0.3 mgm. per 100 cc.

Nicotinic acid—The mean of sprue patients, following administration of 500 mgm. of nicotinic acid is somewhat higher than that of the deficiency group but both were considerably lower than normal controls.

Riboflavin—The mean of patients with sprue was definitely lower than that of patients classified as having a vitamin deficiency and both were significantly lower than that of the normal control group.

Thiamin—During the control period of thiamin excretion the distribution of values between the groups was essentially the same as in the case of riboflavin. After intramuscular injection of 1 mgm. of thiamin the means of excretion levels were the same in sprue patients as in those with a vitamin deficiency.

Single deficiencies are rarely if ever seen clinically. In sprue anorexia, diarrhoea and interference with absorption determine multiple vitamin deficiencies. This has already been noted, except in the case of nicotinic acid. A possible explanation may lie in the wasting with destruction of body tissues which would afford a certain amount of nicotinic acid for utilization by the body.

Fats are poorly absorbed in sprue so that vitamin A and carotene, being fat-soluble are lost. It might be supposed that the diarrhoea alone is responsible for these low levels, but a comparison with patients having amoebic dysentery shows that this is not the case. In eight patients with amoebic dysentery the mean blood plasma-level of carotene was 141 I.U. as compared with a mean of 50 I.U. in the sprue group which would suggest that carotene is absorbed in the small intestine. There is likewise a striking difference between carotene and vitamin A levels in sprue as compared with those in pernicious anaemia in which they are much higher. The striking differences in distribution and means of vitamin A and carotene suggest that these determinations may prove useful as an aid in the diagnosis of sprue and its differentiation from pernicious anaemia.

P. Manson-Baker

REWELL, R. E. A Case of the Sprue Syndrome of Unusual Aetiology. *Guy's Hosp Reports* 1944 v 83 (v 23 4th ser.) Nos 3-4 74-8 2 figs on 1 pl. [13 refs.]

HAEMATOLOGY

BROWN, A. Clinical Haemoglobinometry. *Glasgow Med J* 1945 Aug v 26 39-43 [12 refs.]

The evolution of the technique of clinical haemoglobinometry is reviewed briefly and attention is drawn to the widely varying standards of normality that have been adopted by the earlier workers.

Twenty Sahli haemoglobinometers in general use in a large teaching hospital were checked against an accurate photoelectric method, and readings for 100 per cent. were found to vary from 10.4 to 17 gm. of haemoglobin per cent. This variation was not entirely due to faulty replacements in old apparatus since "manufacturers appear to have their own ideas with regard to normal haemoglobin levels."

The author deprecates the expression of haemoglobin values as percentages of an arbitrary normal.

[The inaccuracy of many haemoglobinometers in general use is of course now being widely recognized. To some extent this fault is being rectified by the adoption of the specifications for the Haldane instrument recently published by the Medical Research Council's Committee on Haemoglobin Surveys. If haemoglobinometers manufactured according to such specified standards be used it is difficult to see why the readings should not be expressed as percentages of normal provided that the equivalent of 100 per cent in terms of grammes of haemoglobin per 100 cc. of blood is known.]

L. J. Davis

MOLT, R. H. Diurnal and Sampling Variations in the Determination of Haemoglobin. *J. Physiology* 1945 June 29 v 104 No 1 1-5

Various reports of repeated haemoglobin determinations on the same individual have shown considerable variation during the course of a single day. With the object of determining whether such variability is due to sampling and technical errors or to a true diurnal variation the statistical method of variance analysis has been applied to an examination of certain careful observations previously recorded by MCCARTHY and VAN SLAKE (*J. Biol. Chem.* 1939 v 128 567) who used the carbon monoxide capacity method for haemoglobin estimation.

It is concluded that between 9 a.m. and 11 p.m. there was a significant fall in haemoglobin of about 4 per cent but that there was no significant diurnal change during the working day from 9 a.m. to 5 p.m.

It is also pointed out that if the diurnal variation is disregarded and included in the random variability the standard deviation of repeated estimations is 0.54 vol. of carbon monoxide. On the normally accepted basis of twice the standard error this means that there must be a difference of nearly 8 per cent between two haemoglobin estimations on one individual before this difference can be attributed with safety to anything but experimental error. In most experimental and clinical work where haemoglobin measurements are used to assess an experimental or therapeutic procedure there will be at least as big an experimental error as this against which changes in haemoglobin must be interpreted. The magnitude of sampling and diurnal variations sets a limit too beyond which it becomes no longer useful to increase the accuracy of haemoglobinometer readings. The limit is reached when the standard deviation of repeated measurement is about 1% on Haldane's scale.

L. J. Davis

BROWN, A. & ANDERSON, A. B. The Photoelectric Estimation of Haemoglobin. *Glasgow Med. J.* 1945 Aug v 26 44-9 [21 refs.]

After a short critical review of current methods of haemoglobinometry a description is given of the author's technique of haemoglobin estimation with a photo-electric colorimeter. The calibration of this instrument by oxygen capacity of the blood is described, and the results obtained on a series of blood samples varying in haemoglobin content from 6.6 to 16.3 gm. per 100 cc. were found to be in very close correlation with those obtained by the direct estimation of oxygen capacity.

L. J. Davis.

CASE, R. A. M. Siderocytes in Haemolytic Diseases: a New Index of Severity and Progress. *J. Path. & Bact.* 1945 Apr v 57 No 2, 271-3 [14 refs.]

Siderocytes are erythrocytes containing fragments of non haematin iron. They were so named and brought into prominence by GRUNBERG (*Nature* 1941 July 26 114 & Oct 18 469) and have been reported in certain pathological conditions. The author has previously described a new and delicate staining

technique with α dipyritydyl and potassium thiocyanate and has shown that the siderotic granules are eventually extruded giving an increase of plasma iron, that the cell after extrusion of the granules is susceptible of phagocytosis and that the onset of a high siderocyte level is accompanied by the appearance of urinary siderotic granules. It was therefore inferred that siderocytes might be increased in haemolytic conditions.

The present communication records siderocyte counts in a variety of conditions, including those characterized by excessive red cell destruction. In normal individuals the siderocyte count was from 0.5 to 0.8 per cent. in hypochromic microcytic anaemia from 1 to 3 per cent. whereas in various types of haemolytic anaemia it ranged from 10 to 100 per cent. In untreated pernicious anaemia, counts of 8 to 14 per cent. were recorded but during the course of therapeutic remission they fall to normal levels.

It is concluded that the siderocyte count may be a sensitive and useful guide in assessing the severity and progress of haemolytic conditions.

L. J. DARRIS

WINSON, T & BURCH, G. E. Habitus of Patients with Active Sickle Cell Anemia of Long Duration. *Arch Intern Med* 1945 July, 76, No. 1 47-53 7 figs. (Refs in footnotes)

The authors hold that patients with long-standing sickle cell anaemia have a fairly characteristic habitus which may be considered typical of the disease and that awareness of this habitus may lead to the disease being suspected on inspection of the nude patient.

Such patients are slender and appear relatively tall although they are not necessarily of greater than average height. The shoulders and hips are narrow producing a linear type of habitus. In some the head is somewhat abnormal in shape being dolichocephalic scaphocephalic or otherwise unusual. The neck appears short. The normal upper dorsal kyphotic curvature is definitely accentuated and the lower lumbar curvature excessively lordotic. The arms and legs are thin and long and the trunk is short. The chest is deep and narrow producing a hoop-chested appearance. The hands and fingers, feet and toes are long and narrow the hands have been well termed spider hands. Signs of hypogonadism, such as genital hypoplasia or atrophy, hypotrichosis and high pitched voice are encountered occasionally. In children the signs are either slightly or strongly abnormal depending on the severity and duration of the disease thin arms and legs, hoop chest and protruding abdomen being the most outstanding characteristics.

X-ray abnormalities are not constant. Changes in the skull are rare and consist of decalcification with exaggeration of the normal reticulation, best seen in the vertex. The vertebral bodies sometimes show pronounced decalcification, and sometimes crescentic depressions of their superior and inferior borders most noticeable in the lumbar region. The hands show "spider fingers" with pronounced decalcification in the metacarpal bones and phalanges in some cases.

Anthropometric measurements showed that the mean stature of the diseased patients was slightly less than that of control subjects and that the mean weight of the patients was noticeably less. The span was less for patients than for the controls but the relation of the span to stature was not significantly different in the two groups. Compared with stature the sitting height was shorter while the average pubic height was greater in the patients than in normal persons. The average widths of the shoulders and pelvis were less in the diseased group than in the control, as were also the circumferences of the chest and abdomen. The antero-posterior diameter of the chest was relatively increased in the patients.

The anaemia is probably of great importance in altering the habitus as patients with sicklaemia but no anaemia do not have an abnormal habitus.

The habitus of the normal adult American negro may be confused with that of those suffering from sickle anaemia. The normal negro is of short light and slender build the span exceeding the stature by as much as 12 cm in some negro men. The habitus of patients with sickle cell anaemia also superficially resembles that encountered with primary hypogonadism. In sickle cell anaemia however the span does not exceed 107 per cent of the stature whereas in primary hypogonadism the ratio may exceed 112 per cent. In sickle cell anaemia the stature is often less than normal while in primary hypogonadism it is greater than normal. The body weight in primary hypogonadism is not usually abnormally decreased but in sickle cell anaemia it is usually sharply reduced. In both diseases the trunk is short compared with the stature but in primary hypogonadism this is due to definite overgrowth of the long bones whereas in sickle cell anaemia it is due mostly to decrease in height of the lumbar vertebrae. In sickle cell anaemia some of the adult patients with severe anaemia have evidence of gonadal hypofunction but this is a secondary and not a primary type. *I. Murgatroyd*

TOMLINSON W. J. Abdominal Crises in Uncomplicated Sickle Cell Anemia. A Clinico-Pathologic Study of 11 Cases with a suggested Explanation of their Cause. *Amer J Med Sci* 1945 June v 209 No 6 722-41 1 fig [29 refs]

With a view to throwing light on the causation of abdominal crises in sickle cell anaemia a study was made of the clinical and autopsy findings in eleven cases showing this complication which had been admitted to the Gorgas Hospital in the Panama Canal Zone.

Four of the patients were dead before they were seen by a physician. In the remaining seven the illness terminated fatally and manifestations of shock were recorded in five. The clinical picture was characterized by sudden abdominal distress with rigidity pain or tenderness rigors frequently jaundice and peripheral vascular collapse. Severe anaemia was a constant feature but since haemoglobinuria was absent the anaemia was not thought to result from intravascular haemolysis.

The evidence of shock was found post mortem in all cases the peripheral veins being collapsed and the internal organs showing marked congestion.

It is suggested that the mechanism of death in these cases is shock and that the anoxia is aggravated because the sickled erythrocytes are ineffective carriers of oxygen and because they tend to stagnate in the small capillaries thus increasing the circulatory failure and perpetuating the vicious circle of shock.

The desirability of treating such cases with blood or plasma transfusions is emphasized but attention is drawn to the necessity of rejecting donors who show the sickling trait. *L. J. Davis*

TRINCAO C. The Sickle-Cell Trait in Saint Thomas Island. *An Inst Med Trop Lisbon* 1944 Dec v 1 No 2, 391-2.

TEIXEIRA W. G. Hematias falciformes nos indigenas de Angola. [Sickle Cells in the Natives of Angola] *An Inst Med Trop Lisbon* 1944 Dec v 1 No 2 385-74 2 figs on 1 pl. English summary (9 lines)

SARMENTO A. Contribuição para o estudo da anemia de células falciformes nos negros de Angola. [Contribution to the Study of Sickle Cell Anaemia in the Negroes of Angola] *An Inst Med Trop Lisbon* 1944 Dec v 1 No 2 345-50 English summary (6 lines)

VENOMS AND ANTIVENENES

BOQUET P. Sur la toxicité du sérum de *Lipera aspis* [The Toxicity of the Serum of *Lipera aspis*] *Ann Inst Pasteur* 1944 Sept. Oct v 70 Nos. 9-10 302-4

PHIALIX and BERTRAND have stated that the serum of this viper is toxic by reason of the presence of the parotid gland venom in the blood. CALMETTE, ARTHUR and others have disputed this. The author has consequently estimated the toxicity of *L. aspis* venom and serum *in vivo* and their diastatic activity *in vitro*.

A minimum dose of 0.35 mgm. of the venom per kgm. body weight intravenously injected kills a rabbit in 3-5 minutes all the blood in heart and vessels being coagulated. For guinea-pigs of 450 gm. weight and the same venom similarly administered a dose of 0.1 mgm. is needed, and the blood in heart and vessels is fluid and not coagulable. If 1.5 mgm. are injected subcutaneously into a guinea-pig there is local oedema and sloughing and death ensues in about 24 hours. Intraperitoneal injection of 0.03 mgm. into mice of 18-20 gm. kills in a few hours the blood remaining fluid. Heating the venom to 60°C. reduces slightly its toxicity for the guinea-pig but not for the other animals.

Fresh serum is much less toxic than the venom. At least 6 cc. intravenously are needed to kill a rabbit of 2 kgm. in an hour and the blood coagulates only slowly after death. When the serum has been heated to 56°C. for 30 minutes it loses its toxic properties. One cc. of fresh serum killed most guinea-pigs in less than an hour but some lived longer. At autopsy the viscera were very congested and showed focal haemorrhages. The blood is partly haemolyzed and coagulates slowly. Subcutaneously administered 1 cc. causes in 24 hours local oedema followed by necrosis. 0.1 cc. of the serum injected intraperitoneally into a mouse causes death in a few hours but even five times this dose has no toxic effect if the serum is heated to 56°C.

In vitro the venom is found to haemolyse horse red cells by action of a lipodase in presence of lecithin and to coagulate the plasma. Heating to 60°C. does not affect these actions. The serum does not coagulate horse plasma, but haemolyzes the red cells directly without any need for added lecithin and heating to 56°C. for 30 minutes inhibits this action.

If the serum contained venom as it is secreted by the glands the toxic effect should be inhibited by antivenene but it is not.

H. Harold Scott

DERMATOLOGY AND FUNGUS DISEASES

D. AVANZO C. S. Impetigo Bullosa in the Tropics. *Arch Dermat & Syph* 1945 July v 52 No 1 23-9

Impetigo bullosa is one of the more common dermatologic entities found among troops in the tropics particularly in the infantry. The eruption appeared in 0.7 per cent of all troops observed. Most patients with impetigo bullosa were treated in their units satisfactorily. They constituted 0.44 per cent of all admissions and 3.2 per cent of those hospitalized for cutaneous diseases. The most important factor involved in this disease is perspiration. Although it is less frequent, the incidence rate of impetigo bullosa parallels that of malaria, because the same factors help produce both eruptions. Impetigo bullosa as found in the tropics should be removed from the classification of the impetigo

contagiosa group. It is a clinical entity and sweat is the all important factor. The most important part of treatment is prophylaxis. Proper personal hygiene is essential. The commanding officer of the unit has a definite function in prevention and much will depend on him particularly in infantry troops or other troops that do heavy manual labor. Clothing made of light porous material with a coarse weave is recommended for the use of troops in the tropics.

HARPER A R. *Pyoderma in the Tropics with a Description of Three Cases*. *J Roy Nav Med Serv* 1945 July v 31 No 3 170-72.

McLAUGHLIN R R M. *Treatment of Tropical Skin Diseases in the South Pacific an Outline*. *U S Nav Med Bull* 1945 Aug v 45 No 2 314-22.

The author records his opinions concerning some 5 000 dermatological cases seen during the course of medical duties with the U S Navy in the South Pacific. Of these cases 33 per cent were suffering from fungous infections 15 per cent from pustular or cystic acne 10 per cent from ulcers of various types 10 per cent from dermatitis venenata (tropical woods or foliage) and about 6 per cent from impetigo and ecthyma.

The main part of the communication consists of direct and sensible instruction concerning the treatment of the commoner cutaneous diseases but there are two points which attract the abstracters attention. The first is the recommendation to treat pediculosis pubis by spraying the infested area with Treon Aerosol Insecticide the second is the author's insistence that contrary to popular belief pustular and cystic forms of acne vulgaris are aggravated by tropical service and that this eruption may develop in hot climates in men who have not previously suffered from the malady.

[Without doubt the author is correct in his thesis that under conditions of active service in hot and—ono may add—humid climates acne vulgaris may be severely aggravated. He may also be quite correct in his assertion that the eruption may develop *de novo* in adult males working in such areas some would maintain that any adult over say 25 years of age who suddenly develops severe acne in the tropics probably suffered from the eruption in a sub-clinical form in adolescence.]

R M B McKenna

SOBERÓN Y PARRA G & LEÓN Y BLANCO F. *Las moscas del género Hippelates como posibles vectores del mal del pinto* (2a. comunicacion). [*Flies of the Genus Musca as possible Vectors of Pinto.*] *Ciencia Mexico* 1944 v 4 No 11/12 299-300. [Summary taken from *Rev Applied Entom Ser B* 1945 Aug v 33 Pt 8 125.]

The authors refer to experiments in Mexico described in a paper that has not been received at this Institute (F LEÓN Y BLANCO & G SOBERÓN Y PARRA. *Nota sobre la transmisión experimental del mal del pinto por medio de una mosca del género Hippelates*. *Gac méd Méx* 71, pp 534-539 1941) in which they showed that the disease known as mal del pinto [or carate] could be transmitted by flies of the genus *Hippelates*. An account is given in the present paper of investigations on the persistence of the spirochaetes [*Spirochaeta carateae*] in flies of this genus that had fed on serum from an opened lesion on an infected person. Mobile spirochaetes were present in all cases in serum from the digestive tract of the flies 10-30 minutes after an infective meal spirochaetes were in all cases present but some had lost their mobility 40-70 minutes after the meal and fewer could be seen and most were motionless after 80-120 minutes. Only very occasional motionless spirochaetes were seen when more than two hours had elapsed. There were spirochaetes in three out of 11 specimens of vomit drops each from 4-10 flies, collected 15-20

minutes after an infective meal and examined immediately. No spirochaetes were found in the contents of the digestive tract of 31 adult *Hippelates* taken in nature.

DI PIETRO A. Granuloma nasal a *Rhinosporidium seberi* (8a observación argentina)
[Nasal Granuloma due to *R. seberi*] *Rev. Asoc. Med. Argentina* 1945 June 30
v. 59 No. 580 "04-" 6 fig.

SULZBERGER M. B. SHAW H. C. & KANOF A. Evaluation of Measures for Use against Common Fungous Infections of Skin. Screening Tests by means of Paired Comparisons on Human Subjects. *U.S. Nav. Med. Bull.* 1945 Aug. v. 45 No. 2, 237-48.

In this paper the authors record the result of an investigation made amongst a controlled population in a Naval Disciplinary Barracks to determine the efficacy of five different medicaments in the prophylaxis of fungous infections of the feet and groin. In all 808 volunteers were used for the experiment, which was made during a period of 3-4 months in 1944.

The materials investigated were —

- Undecylenic acid-zinc-undecylenate powder
- Sodium propionate powder
- Boric acid-salicylic acid powder
- Undecylenic acid-zinc-undecylenate ointment
- Clothing impregnated with Impregnate CC3 by an oil in water emulsion process. The formula of CC3 is not stated. The formulae of the powders and ointment were as follows:—

Propionate powder (pigmented)

	Per cent.
Sodium propionate (du Pont M coban 7)	20.0
Talc, U.S.P.	79.5
Polychloro copper phthalocyanine (green)	0.5

Undecylenic acid-undecylenate powder (pigmented)

	Per cent.
Zinc undecylenate	20.0
Talc, U.S.P.	78.0
Undecylenic acid, Grade AA	2.0
Dibenzothio indigo (red)	2.0

Boric acid-salicylic acid powder (pigmented)

	Per cent.
Salicylic acid, U.S.P. powder	2.0
Boric acid, U.S.P. impalpable powder	6.0
Zinc stearate, U.S.P.	3.0
Talc, U.S.P.	86.5
Dibenzothio indigo (red)	2.0
Polychloro phthalocyanine (green)	0.5

Undecylenic acid-zinc-undecylenate ointment (pigmented)

	Per cent.
Undecylenic acid, Grade AA	5.0
Triethanolamine	3.0
Zinc undecylenate	18.0
Propylene glycol, N.F.	19.0
Carbowax 1,500	39.0
Carbowax, 4,000	29.6
Water distilled	13.0
Dibenzothio indigo (red)	0.4

Experiments in prophylaxis were limited to the protection of the feet from fungous infections. 567 men who were free from active infection of this type were divided into five groups. One group was used as a control and did not receive treatment. four groups were treated as follows —

Group A — Undecylenic acid undecylenate powder for the right foot
boric and salicylic acid powder for the left foot

Group B — Sodium propionate powder on the left foot boric and salicylic acid powder on the right foot

Group C. — Undecylenic acid-undecylenate powder on the right foot
sodium propionate powder on the left foot

Group D — A sock impregnated with CC3 on the right foot no treatment to the left foot

In the control group 8.85 per cent. of the unprotected feet developed fungous infection. The percentage ratios of feet which became infected during the period in which the various prophylactics were used were as follows —

1.07 per cent. treated with undecylenic acid-undecylenate powder

3.10 per cent. treated with sodium propionate powder

8.93 per cent. clothed with socks impregnated with CC3

11.15 per cent. protected with boric and salicylic powder

Therefore in this investigation the undecylenic acid and the sodium propionate powders gave the best protection whilst the use of impregnated socks or boric and salicylic acid powder appeared not to confer benefit to the users.

With regard to the apparent advantages of the use of the undecylenic acid preparations and the propionate powder the authors are not prepared to say more than that they appear to afford some degree of protection against fungous infections of the feet the former powder being perhaps somewhat superior to the latter.

When the preparations were used for the treatment of active fungous infections of the feet (160 persons) and groin (72 persons) undecylenic acid-undecylenate powder and sodium propionate powder were found to be effective on both areas the former being more effective than the latter particularly in the crural area. Undecylenic acid-zinc undecylenate applied to the feet in an ointment vehicle was not superior to the same ingredients incorporated in a powder. Shorts and socks impregnated with CC3 did not produce any significant therapeutic effect the shorts produced irritation of the skin in about one-third of 11 patients who wore them.

The authors found that in six cases of pityriasis versicolor the use of undecylenic acid-zinc undecylenate ointment and propionate acid-sodium propionate ointment failed to produce any therapeutic response they suggest that this may be associated with the preference shown by the causal fungus (*Microsporon furfur*) for cutaneous areas where the sweat is more acid for this preference may indicate that the fungus has an inherent resistance to fatty acids and their salts.

[Besides the findings stated the communication has many points of interest. The authors are extremely conservative they claim nothing more than that the results are sufficiently encouraging to warrant field trials of the better preparations. Their technique of using paired comparisons on human subjects is of interest and the device of giving each preparation a distinctive colour is an ingenious method of circumventing human fallibility. They emphasize that for practical purposes powders are preferable to ointments.

The investigation seems to have been well controlled. It is interesting to note that although numerous patch tests of the ingredients used failed to produce any cutaneous reactions (although in many instances the tests were repeated twice with an interval of four weeks between them) impregnated

shorts caused irritation in about one-third of the wearers. It has been found in Britain, in the investigation of cases of textile dermatitis that patch tests made with the suspected material frequently fail to produce any reaction in the skin, whilst wearing of the suspected garment may rapidly produce a cutaneous inflammation. Also it may be noted that, in infections of the groin, the undecylenic acid powder and the propionate powder required an average period of 3.5 and 5.5 weeks respectively to produce a cure—this is a slow rate of therapy. The time factor was more satisfactory with regard to the feet, cure being obtained with both preparations in 4-6 weeks.

This communication may be integrated with the papers by KEENEY AJELLO and LANKFORD published in the *Bull Johns Hopkins Hosp* 1944 v 75 pp 377-393 and 410.

R. M. B. Mackenna

TROPICAL OPHTHALMOLOGY

A REVIEW OF RECENT ARTICLES XLVI.*

Conjunctivitis.—The treatment of acute conjunctivitis and trachoma with sulphonamides is discussed by MITCHESTER and STERN.¹ During the 1941 summer epidemic of Koch-Weeks conjunctivitis they examined the use of sulphanilamide and some of its derivatives in the local and oral treatment of this disease. Koch-Weeks conjunctivitis in the Near East appears in epidemic form in the summer and early autumn and affects children especially. It is highly contagious, usually attacks both eyes and is characterized by a profuse discharge with much swelling of the eyelids and conjunctiva. The authors started their experiments with Pyranil (Teva Ltd) which had shown strong bactericidal activity *in vitro* and *in vivo*. Pyranil is a compound containing *p*-aminophenyl-sulphonamide (sulphanilamide) in addition to pyridine-dicarboxylic acid anhydride. An ointment was prepared which contained 5 per cent. of the active principle in an adequate ointment base. In 13 cases of Koch-Weeks conjunctivitis, one eye was treated with Pyranil ointment and the other with 2 per cent. silver nitrate. The results in 12 cases were equally good in both eyes. In a few more cases of Koch-Weeks conjunctivitis both eyes were treated with Pyranil ointment as well as with silver nitrate. The combination gave excellent results and encouraged them to try sulphanilamide and sulphapyridine by the mouth. The former had no effect but the latter given by the mouth without any local treatment cleared up the conjunctivitis completely in so short a time that treatment with silver nitrate seemed slow in comparison. About 50 cases of all ages were treated and the following course gave the best results. A total of 0.05 gm. per kgm. body weight per day is given in divided doses. The intervals must not be too long; every 2-3 hours seems to be the best interval. On the 2nd and 3rd day this dosage is repeated. During the next 4-5 days, it is gradually diminished. If slight swelling and injection of the conjunctiva remains, treatment is to be continued with argyrol noviform ointment or some other antiseptic ointment. In the treatment of trachoma, including the corneal complications the authors obtained excellent results with pyranil ointment, and in severe cases resisting every therapeutic attempt, this ointment is the treatment of choice though it does not exclude the use of atropine and sulphanilamide by mouth or make it unnecessary to squeeze out trachomatous granules if they need it.

For the 45th of this Series see Vol. 42 pp 486-490.

¹MITCHESTER B. & STERN H. J. Treatment of Acute Conjunctivitis and Trachoma with Sulphonamides. *Lancet* 1945 May 26 649-50 2 figs.

The effect of various dosage with sulphapyridine sulphathiazole sulphadiazine and penicillin in the treatment of the acute epidemic ophthalmias (Koch Weeks and gonococcal) of Egypt was studied by BLAND and WILSON.² They found that a single dose of a sulphonamide will cause a reduction of bacteria in four hours and total suppression of bacteria in about 12 hours. A considerable proportion of gonococcal cases will be cured by a single dose but Koch Weeks cases are more resistant. Two doses on two successive days (3 doses in all) will cure all cases of gonococcal and Koch Weeks ophthalmia with very rare exceptions. A single intramuscular dose of penicillin will reduce gonococci to nil in 3-4 hours but repeated doses at short intervals are necessary to ensure cure. Relapses occur in 10-12 hours after a single dose. Penicillin has no effect on Koch Weeks cases and is therefore unsuitable as a treatment for acute Egyptian ophthalmia.

Those who know the conditions of life in Egypt and other oriental countries where similar conditions of life and disease prevail will realize the importance of these findings. Acute ophthalmia is the cause of 80 per cent of the blindness (total blindness 1 per cent monocular 4 per cent) of Egypt. The increased ocular secretion caused by the disease promotes also the spread of trachoma that second universal plague of Egypt itself a fertile source of damaged sight. The authors point out that no treatment which requires hospitalization or even attendance at hospital can hope to do more than scratch the surface of this problem of eye disease unless treatment can be taken to the villages where the great majority of the people live and there simply and easily administered. They believe the treatment with sulphonamides provides the necessary solution as it is simple safe effective and could be given by unqualified persons with a minimum of training.

GUTMANA³ writing on allergic warm season conjunctivitis considers that conjunctivitis vernalis (spring catarrh or vernal conjunctivitis) as seen in Palestine is badly named in that the name is not sufficiently comprehensive it would be more appropriately called an allergic warm season conjunctivitis (a.w.s.c.). The experiments he reports are based on 180 cases, 36 of whom were examined and treated by the author over the last eight years. An analysis of the age of patients showed 10.5 per cent have been between 1-5 years 24 per cent between 5-10 years 21 per cent 10-15 years 7.5 per cent between 15-20 years 28.5 per cent between 20-30 years and 7.5 per cent 30 years and more. He found that the disease is three times as common in males as in females and that girls very seldom contract it. He considers that hormonal factors may be of importance and that the combination of heat and moisture are the climatic factors responsible for the condition.

Allergic warm season conjunctivitis (spring catarrh) has nothing to do in any way with hay fever although in patients with a.w.s.c. he found allergic reactions to bacterial allergens and moulds (fungi). The average of the blood eosinophiles was 9.6 per cent there were numerous eosinophilic cells in the lacrimal secretion the blood sedimentation rate and the blood calcium level were normal. More than half the patients had suffered previously from other allergic diseases and hereditary cases were often seen. The allergic skin reaction to moulds is similar to that for bacterial allergens namely the late reaction but this is not exclusively so and the patients may show the nodular typical lagging reaction. The a.w.s.c. appears as a secondary allergic disease the primary cause of which is to be sought in some sort of chronic infection such as

²BLAND J. O. W. & WILSON R. P. Bacteriological and Clinical Observations on the Treatment of the Acute Ophthalmias of Egypt with Sulphonamides and Penicillin. *Brit J Ophthalmology* 1945 July v 29 No 7 339-55 [10 refs.]

³GUTMANA M. J. Allergic Warm Season Conjunctivitis (Conjunctivitis Vernalis Spring Catarrh, Vernal Conjunctivitis) as an Allergic Disease. *Acta Med Orientalis (Palestine & Near East Med J)* 1945 May v 4 No 5 150-55 [16 refs.]

infected teeth tonsils, sinuses etc. upon which a fungal allergy is superimposed. The fungi most frequently found were *Alternaria* *Hormodendron* and *Cladosporium* *Penicillium* *Aspergillus* *Monilia* and yeasts.

Treatment consists in the removal of foci of infection and in reorganization of the patient's surroundings. For desensitization a mixed extract of various moulds from the material of the patient's surroundings fortified by bacterial allergens is used. All infections are given intracutaneously for at least six months and in most cases for 1-2 years.

Trachoma—Mass education, school medical services, and defective vision with special reference to trachoma in East Africa are discussed by Howard REED. The pamphlet entitled "Mass Education in African Society" (Colonial No 186) which has been published by the Advisory Committee on Education in the Colonies is of great interest to all concerned with post war development in our African colonies. Two main lines of attack are suggested—the provision of schools so that children may receive the rudiments of learning and the fostering of voluntary groups with the provision of literature in the native language so that young literate people may be helped to continue their education after leaving school. The most effective way of assisting mass education is to concentrate upon cultivating a state of positive health in schoolchildren by developing an efficient school medical service in which the care of eyesight plays a very important part. Inability to see clearly prevents accurate observation, and eye-strain caused by visual defects induces a distaste for learning. Medical inspection and treatment of schoolchildren should provide for routine eye examinations. External diseases of the eyes such as conjunctivitis and corneal ulceration are prevalent in the tropics and cause much defective vision. Of these trachoma is far the most important and its aetiology still remains unknown. The present incidence of trachoma in the East African colonies is very difficult to estimate with any degree of accuracy but there is no doubt that it is more widespread than is generally realized. According to Jones the percentage of trachoma cases in Uganda schools is 13 and according to Boase it is very prevalent in Uganda. Harley Mason gives the percentage of trachoma cases attending the Nairobi Eye Clinic for 1941-43 as 12 to 17 per cent. In Mwanza the author found that in 232 native eye cases 21.5 per cent were undisputable cases of trachoma. Wilson working in Masailand says the disease is common. McDonald found in Lindi that trachoma was the chief cause of rejection of recruits. Out of 4,000 men examined in 1943 there were 23.3 per cent rejected for trachoma. In Egypt where trachoma is so widespread MacCallan found that very heavy infection occurred in pockets. An irregular distribution has also been found in India, and it is probable that when a survey is made in East Africa, the degree of trachoma infection will vary greatly in different areas. It would appear that the trachoma at present seen in East Africa is of a less virulent type than that seen in Egypt and India.

The author issues a warning that a post war increase of trachoma in East Africa may follow the return of the East African troops. This would be due to the large scale movements of African troops and labour corps to the Middle East and Far East in which areas the incidence of trachoma is high, and would necessarily cause a corresponding adverse effect upon the execution of the plans for mass education. The following methods might be adopted to estimate the danger of an increase of trachoma after the war—

1. The present incidence of trachoma in East Africa should be estimated. This could most accurately be done by the examination of the eyes of school-children in given areas.

¹ Reed H. Mass Education School Medical Services and Defective Vision, with special reference to Trachoma in East Africa. East Afric Med J 1945 Feb v 22 No 2, 48-55.

2. The Army Medical Services should be requested to make a special investigation and to supply statistics of the degree of infection among East African troops. This should be carried out by a medical officer having special knowledge of trachoma.

To combat trachoma the following measures might be introduced —

1. Regular medical inspection of schools including village schools, circular giving an account of the disease and its treatment could usefully be issued to all medical officers.

2. Children are usually infected during the first two years of life so that early cases could be reached to some extent by giving instruction in the diagnosis of the disease to health visitors and those connected with child welfare and maternity clinics. In these clinics infected mothers could be discovered, treated and rendered less infectious when the baby is born.

3. The daily administration of eye-drops to infected schoolchildren by the teachers until such time as a school medical service is introduced.

4. Special eye clinics should be opened in central towns for treatment as well as for teaching the subordinate medical staff.

5. Africans in the military forces should receive adequate treatment before demobilization to render them non-infectious.

The surgical treatment of trachoma in Uganda is described by BOASE⁶. In a recent sample survey of 504 blind persons in a part of the kingdom of Buganda he found that trachoma was responsible for blindness in 30 per cent of these cases. It is found in all sections of the community in all stages and varies in its manifestations from a type so severe as to ridicule text book descriptions to a type so mild that only a fortuitous examination will disclose its presence. The incidence is markedly affected by standards of hygiene and nutrition. Treatment on classical lines is tedious, painful and prolonged and few persevere to the stage of arrest or cure. The author's method (surgical one) holds a prospect of speedier relief in cases of severe trachoma in stage 2 and in all cases showing trichiasis or entropion. The operation consists of a sub-total resection of the upper tarsal plate (and sometimes the lower). There is nothing original in this procedure — it is sometimes known as Heiars' operation and is described by MacCallan under the somewhat cumbersome title of 'combined excision of tarsus and conjunctiva'. The descriptive term 'tarsectomy' is widely used by other writers and has the advantage of brevity. The following description applies to the author's technique — Surface anaesthesia of the eyeball is obtained with drops of 1 per cent Pantoicaine (or Dicaïne). The lid is infiltrated with 2 cc of 2 per cent procaine-adrenaline solution. The needle is introduced in the centre of the lid and 1 cc injected towards each canthus. Adequate eversion of the lid is essential for facile performance of the operation. This is best fulfilled by Cruickshank's entropion forceps (Down's catalogue 724/7) which is applied solely to the skin of the lid; the spatula blade is placed in the hollow between the globe and the supra-orbital margin and the 3-pronged blade on the lid 2 to 3 mm above the lashes. The forceps is then closed and secured with the fixing screw thus firmly holding a sizeable fold of skin, subcutaneous tissue and orbicularis muscle between the blades. When the handle is depressed towards the forehead the lid is automatically and satisfactorily everted. It is then clipped to the towel with a towel clip to prevent it from flying back towards the cheek. A sharp knife is used to divide the tarsal plate along its whole length at about the level of the subtarsal sulcus. The incision is commenced at the inner canthus for the right eye and at the outer canthus for the left eye and is

⁶BOASE A. J. The Surgical Treatment of Trachoma. *East African Med J* 1945 Feb v 22, No 2 58-61.

extended across the lid, keeping about $1\frac{1}{2}$ mm. from the margin. The section must be made with small sawing movements as the average trachomatous tarsus is very dense. It is of paramount importance to keep the line of the incision at a uniform distance from the lid margin. The tarsus is now seized with a fixation forceps or a small vulsellum at the centre of the proximal lip of the incision and with a few light strokes of the knife is separated from the overlying tissue. The dissection is continued upwards for 3 to 4 mm. above the upper edge of the tarsal plate so as to mobilize the conjunctiva in this area. This is more conveniently done with scissors. The next step is to cut through the conjunctiva as close as possible to this upper edge. Haemorrhage may be a nuisance but is easily controlled by twisting off the severed vessels. Three 8-inches long double-armed cotton thread sutures on No. 3 or 4 half curved needles are required. The cut edge of the conjunctiva is seized at its centre and pulled down. One needle of the double-arm suture is passed through the conjunctiva from its superficial aspect close to the cut edge and then through the lid just above the stump of the tarsus so that it emerges on the skin close to the middle prong of the eversion forceps, that is 2-3 mm. above the lashes. The second needle of this suture is then passed through the stump of the tarsus and out through the skin 1 mm. or so nearer the lashes than the first needle. The remaining two double-arm sutures are inserted in a similar manner on either side of the central one and at points half way between it and the canthi. The eversion forceps is now removed and the lid allowed to fall into place. The sutures are pulled taught and after the cut edge of the conjunctiva has been adjusted to that of the tarsal stump they are tied over a thin strip of rubber dam which facilitates their subsequent removal. With practice the operation can be performed on both eyes in the space of 15 to 20 minutes.

[The reviewer with a large experience of trachoma, agrees with MacCallan that the operation of tarsectomy is unsuitable for the relief of simple trichiasis and should be reserved for cases of trachoma stage 2 where there is gross shaggy papillary hypertrophy of the conjunctiva. Webster's mucous graft operation is a very satisfactory one for the varying degrees of trichiasis-entropion.]

The aetiology of trachoma is critically reviewed by BLAND* and in the course of this review he points out that the four cardinal diagnostic signs of trachoma in man are The presence of inclusion bodies the formation of follicles on the tarsus vascularization of the cornea and scarring of the conjunctiva. The available evidence shows that trachoma is a specific infectious disease caused by a non-cultivable filterable agent identical with the elementary and initial bodies found in the Prowazek Halberstaedter inclusions and bearing a close natural relationship to the viruses of inclusion conjunctivitis, lymphogranuloma inguinale and psittacosis. There is no evidence that this agent possesses an arthropod host nor that the louse is a vector of the disease though the agent may survive for some days in the body of the louse. Are we to consider the trachoma agent along with the three other agents to which it is related, as rickettsiae or viruses. Since at present there is not complete agreement among bacteriologists as to the precise definition of the genus *Rickettsia* and since the virus group is largely defined by negative characteristics and possibly contains agents of very different intrinsic nature which a natural biological classification would not place together the matter becomes largely one of personal choice. Undoubtedly, these four agents resemble the rickettsiae in a number of points they are minute in size and show pleomorphism, though not the bacillary and thread forms of typical

*BLAND J. O. W. The Aetiology of Trachoma. A Critical Review of Present Knowledge. *Brit. J. Ophthalmol.* 1945 Aug. v 29 No 3 407-29 [38 refs.]

rickettsiae they do not stain with aniline dyes they are Gram negative they stain easily with Giemsa and in their various morphological forms take a variety of tints from red to dark blue with this stain they stain easily with Castañeda's stain they are only little if any more filterable than rickettsiae they cannot be cultivated apart from living cells and they adopt an intracellular habitat. Non-cultivability intracellular habitat lack of staining with aniline dyes and Gram negativity are points which are shared both by viruses and rickettsiae. These four agents including trachoma differ from the typical large virus (1) In possessing initial bodies which stain blue with Giemsa and in showing greater pleomorphism (2) in forming inclusions with a basophilic matrix (3) in staining with Castañeda's stain. They differ from typical rickettsiae (1) In lack of an arthropod host (2) in not showing bacillary and thread forms (3) in forming inclusions with a matrix.

The author himself is of opinion that the four agents stand in an intermediate position between the rickettsiae and the large viruses and may possibly form a biological link between them. For the present he prefers to group them with the viruses but to give them a distinctive position as the basophilic viruses on account of the blue staining of their initial bodies and of the matrix of their inclusions which distinguishes them from the larger typical viruses which do not possess blue initial bodies and whose inclusions are acidophilic.

Keratitis—CHAMBERLAIN and BRONSON⁷ working amongst troops exposed to malaria have found an increased incidence of keratitis associated with herpes simplex in a population heavily infected with malaria. Amongst new patients attending the ophthalmological clinic over a period of 18 months there were more than six times the number from a malarial division as from one that had not been exposed to malarial infection. The incidence however is very low less than 0.2 per cent of patients with acute malaria became affected with herpetic keratitis. Early diagnosis and intensive treatment of malaria are essential in the management of herpetic keratitis occurring in patients with malaria. Recurrent attacks of malaria are often associated with a reactivation or an extension of the corneal ulceration.

Sulphadiazine powder applied locally seems to promote rapid healing and the authors suggest that it may prove a satisfactory adjunct to the accepted treatment of dendritic keratitis with strong solution of iodine.

Papillitis—Malarial papillitis amongst the troops in the New Guinea campaign is discussed by LEWY⁸. Although this ocular complication has hitherto been scantily described he considers that it is a common concomitant of recurrent malaria and should be regarded as a papillitis rather than papilloedema because of the injected appearance of the nerve head in the majority of the patients diminution in visual acuity reduced peripheral fields and enlarged blind spots. It is improbable that the condition is a result of medication as none of the patients presented the retinal ischaemia arterial spasm and blindness characteristic of quinine amblyopia which is often the cause of toxic retrobulbar neuritis resulting in complete central blindness and pallor of the disc. There appears to be no direct correlation between the degree of oedema and inflammation of the optic disc and the size of the blind spot neither could any absolute correlation be made between the amount of papillary change and the number of attacks of malaria.

⁷CHAMBERLAIN W. P. Jr & BRONSON L. H. Jr Herpes Simplex Keratitis in Malaria. Clinical and Experimental Study. *Arch Ophthalmology* 1945 Mar; 33 No 3 177-83.

⁸LEWY R. B. Malarial Papillitis. *War Medicine* Chicago. 1945 June v 7 No 6 341-4 3 charts.

Penicillin—The practical uses of penicillin in the everyday practice of ophthalmology are discussed by HARDESTY.⁹ In surface infections, such as conjunctivitis and corneal ulcers, local rather than systemic use was employed, with good results in strengths of 20 000 units per cc. of isotonic salt solution. Two or three drops were instilled into the conjunctival sac every half hour and then every hour. Within 24 hours considerable improvement was noted and within 10 days the eyes were quiet. In cases of non-traumatic orbital cellulitis non-traumatic uveitis and non-luetic keratitis systemic use of penicillin together with appropriate local treatment has proved decidedly beneficial. The author quotes Stokes Sternberg *et al* as having reported improvement in some cases of luetic interstitial keratitis but in the treatment of luetic optic neuritis penicillin should be given with great care as frequent Herxheimer reactions are reported from its use. He also quotes Sievers Knott and Soloway as having reported good results from intramuscular injections of penicillin in gonorrhoeal ophthalmia. In endophthalmitis following penetrating wounds and post-operative intra-ocular infection he advocates daily subconjunctival injections of 0.25 cc. of isotonic salt solution containing 2,500 units of penicillin together with full dosage of the drug intramuscularly. He concludes by saying that with penicillin the practice of ophthalmology has an implement to combat successfully superficial and deep ocular diseases that have heretofore put up a stubborn and unyielding front to all other treatments.

Riboflavin deficiency as a cause of eye disease—Vitamin B₂ deficiency as a cause of eye diseases in Bengal is discussed by KIRWAN SEN and BOSE.¹⁰ In India cases have been reported from Madras but as a result of their investigations the authors found that the incidence of this deficiency in Bengal is low and the occurrence of ocular complications due to riboflavin deficiency is rare. Angular stomatitis, burning sensation in the mouth while taking food fissuring of the tongue seborrhoeic dermatitis of the face with multiple comedones, itching and scaliness of the skin of the scrotum are the main general signs and symptoms.

The ocular manifestations of arboflaviness varied from an itching burning sensation of the eyes to mild or even severe photophobia accompanied by dimness in inadequate light and even to partial blindness. Injection of the palpebral conjunctiva, circumcorneal injection with proliferation of the limbic blood vessels and superficial keratitis were seen in some cases.

The authors are of the opinion that patients with these signs and symptoms are suffering from a deficiency of more than one vitamin.

Blindness and diseases of the eye in South Africa—In an article on this subject BOSHOFF¹¹ points out that there is in existence a very good system for the registration of blind Europeans and that before they become registered for a pension, blind persons must be certified by an ophthalmologist. Hence the causes of blindness are known but these European statistics are not as complete as they should be as self-supporting and non-pensionable blind persons are not on a register of any kind. A Government report (1936) reveals that per 100 000 Europeans in 1908 1911 and 1936 there were 81.24 78.47 and 81.06 blind persons respectively.

Amongst non Europeans the statistics are unreliable and are an understatement of the true facts, as non Europeans can be certified by a district

⁹HARDESTY J. F. The Use of Penicillin in certain Eye Diseases. *Southern Med J* 1945, 38, No. 6, 411-12.

¹⁰KIRWAN E. O'G. SEN K. & BOSE V. Vitamin B₂ Deficiency as a Cause of Eye Diseases in Bengal. *Indian J. Med Res* 1944 Oct, 30, No. 2, 109-15. (33 refs.)

¹¹BOSHOFF P. H. Blindness and Diseases of the Eye in South Africa. *South Africa Med. J* 1945 May 12, 50, No. 9, 148-9.

surgeon. Those placed on the register are only those who actually apply for registration and are fortunate enough to persuade the local native commissioner to grant such a pension. If the blind person's family can support him a pension is not granted. Many persons with curable blindness (such as cataract) fail to seek rehabilitation by surgical means and become a permanent State liability.

For coloured persons there is an incidence of 127.74 blind per 100 000 sighted and partially sighted persons. Amongst the Bantu the incidence of blindness works out to be 400 blind per 100 000 sighted and partially sighted persons. These high figures are upsetting but it is even more alarming to know that in certain districts i.e. North Western Cape, Western and Northern Transvaal the incidence varies from 1 000 to 2 000 blind per 100 000 sighted and partially sighted natives. In Mafeking, Zeerust, Marico and Rustenburg districts the incidence is 1 800 blind per 100 000. The author points out that money would be better spent on preventive work than on providing pensions for the blind. As a result the present expenditure on the blind would be gradually reduced and progress would be discernible. At present not a penny of the pension money is usefully employed. In his opinion the problem of blindness and eye disease in South Africa is desperately bad. Urgent and efficient action is needed. He advocates more interest by Government as to its responsibility in the matter and recommends intensive post graduate training in ophthalmology in the medical school.

Eye Diseases in the East are discussed by MINTON¹² in a brief article. He points out the prevalence of epidemics of conjunctivitis in the Middle East every year in the spring and late autumn. They are of a highly virulent nature and often involve the cornea. They are due to Koch Weeks bacilli, gonococci, diphtheria bacilli and staphylococci. He advocates general treatment with sulphapyridine or sulphathiazole and local treatment with 30 per cent. sulphacetamide drops. He also discusses the prevalence of trachoma and its treatment with the sulphonamides, the presence of vitamin A deficiency in India and Ceylon, epidemic kerato-conjunctivitis during the summer in India. He ends by saying that the incidence of eye infection amongst Europeans living in the tropics is low and that the tropical sun is not harmful to the eyes and is not responsible for eye diseases. E. O. G. KIRWAN

TROPICAL ULCER

PRICE E. W. Spinal Anaesthesia in the Treatment of Tropical Ulcers. *Trans Roy Soc Trop Med & Hyg* 1945 Sept. v. 39 No 1 83-6

Chronic ulcers of the leg as encountered in medical practice in the tropics occasionally resist all the usual methods of treatment. Two such cases in which cure rapidly followed therapeutic spinal anaesthesia are described in this paper.

The first case was in an African boy, aged 14 years, who had ulcers on both feet spreading on to the dorsal and plantar aspects from toes infested with jiggers. He was treated in hospital for six weeks without being cured and was then given an intraspinal injection between the 3rd and 4th lumbar vertebrae of 75 mgm. of procaine in 1 cc. of sterile water and was immediately turned on to his back with his knees drawn up for one minute. Five days afterwards the ulcers were completely healed.

The second case was in an adult leper, aged 25, who had foul-smelling ulcers on the sole of his left foot. After treatment in hospital for 10 days without effect he was given 150 mgm. of procaine in 1.5 cc. of water intraspinally and six days later all the ulcers had healed.

¹²MINTON J. Eye Diseases in the East. *Practitioner* 1945 Sept. v. 155 No. 3 176-9

The author suggests that prolonged arteriolar spasm in the ulcerated area, rather than the presence of endarteritis, causes chronicity of the ulcer. The action of the anaesthetic may be a breaking of a reflex rather than a maintenance of vasodilatation. OCHSNER (*Surgery* 1939 v 5 491) found that paravertebral block with novocain (procaine) immediately relieved the clinical symptoms of thrombophlebitis and the relief was maintained. J F Corson

HAYMOND A. G. Occlusive Dressing—the Almaza Patch. *East African Med J* 1945 July v 22, No. 7 241-2.

An adhesive plaster of Paris dressing, the Almaza Patch was successful in the treatment of sores and ulcers under field conditions in a sandy area. Plaster of Paris three parts tragacanth one part and acriflavine powder 0.001 part were mixed by grinding in a mortar. A piece of open weave bandage a little larger than the sore to be dressed was cut and the powder thoroughly rubbed into its meshes in a mortar. A little of the powder was sprinkled on the sore, then the patch was removed from the mortar with forceps, immersed in enamel or water applied to the sore and carefully moulded with a palette knife the patch was kept at rest until dry and set.

The dressing was left until the sore healed, when it dropped off or became loose. Indolent ulcers were treated with silver nitrate before the patch was applied. The dressing was comfortable did not restrict movement and did not irritate the skin. It was very economical, as an ordinary 50-cigarette tin held enough powder for 500-600 dressings. J F Corson

MISCELLANEOUS DISEASES

GROSFILIZ & LESTIÈRE. Les maladies transmissibles observées dans les colonies françaises et territoires sous mandat pendant l'année 1938. [*Transmissible Diseases in the French Colonies and Mandated Territories during 1938.*] *Ann de Méd et de Pharm Colon* 1940 Apr-May-June v 33 No 2, 183-359.

DICK G. W. A. Routine Stool Examination. *East African Med J* 1945 July v 22 No 7 237-40.

Microscopical examination of the faeces of British African and Italian troops at an East African Casualty Clearing Station showed the following proportions (percentages) of carriers of helminths and protozoa—

Parasite	African (3 000)	British (400)	Italian (400)
	Per cent	Per cent.	Per cent.
<i>Schistosoma mansoni</i>	2.4	0.25	—
<i>Trichostrongylus axei</i>	5.3	1	2.5
<i>Uncinaria stenocephala</i>	4.4	0.25	0.25
<i>Strongyloides stercoralis</i>	5.8	2.3	2
<i>Enterobius vermicularis</i>	0.1	0.25	0.25
<i>Ascaris lumbricoides</i>	2.8	—	0.8
<i>Entamoeba histolytica</i>	9.1	11.3	10.3
<i>Entamoeba coli</i>	9.8	7.5	12.5
<i>Chilomastix mesnili</i>	8.2	11	12.5
<i>Trichomonas hominis</i>	6.4	5.3	6.8
<i>Giardia intestinalis</i>	0.9	2	3
<i>Iodamoeba butschlii</i>	1.6	0.25	1
<i>Endolimax nana</i>	1.8	—	—
<i>Tricostomonas intestinalis</i>	0.2	—	—

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The figures of the Africans suggested that the medical treatment of helminthiasis in the East African Command had been satisfactorily carried out. A cellular exudate characteristic of acute bacillary dysentery was found in 18.7 per cent. of Africans, 16.3 per cent. of British troops, and 16 per cent. of the Italians.

J. F. Corson.

SPÜHLER, O. & KARTAGNER, M. Endemisches Auftreten eosinophiler Lungeninfiltrate in einer militärischen Einheit nebst Bemerkungen über das "miliare" eosinophile Infiltrat. [Pulmonary Infiltration with Eosinophilia in a Military Unit.] *Schweiz med. Woch* 1944, Nov. 4, v. 74, No. 44, 1145-9, 2 figs. [13 refs]

The authors review papers which have been published on the presence of Loeffler's syndrome in association with *Ascaris* infestation, and give notes in tabular form of 28 patients, stating the X-ray appearances of the lungs, the percentage differential leucocyte counts, the presence or absence of *Ascaris* ova in the stools, and the *Ascaris* skin test.

All showed the pulmonary infiltration, but the eosinophilia was not very high, only one reached 35 per cent. *Ascaris* ova were found in the stools of 15, not found in 9 (but one of these had had treatment for ascariasis), in four cases no statement is made [perhaps the stools were not examined in these]. As regards the cutaneous test, in six it was positive and *Ascaris* ova were present; in four it was positive but ova were not seen, in another four the test was negative and no ova were seen, in four the result of the test was negative, but ova were present; in the others the test does not seem to have been carried out, at all events there is no record of it. In spite of these results being so much at variance the authors regard the syndrome as an allergy due to *Ascaris* infestation. [On their own showing in the table, there is as much evidence from these cases *contra* as *pro*.]

H. Harold Scott.

CARDIS, F. A propos de l'infiltrat pulmonaire fugace avec éosinophilie sanguine et de son étiologie le plus souvent vermineuse. [Transient Infiltration of the Lungs with Eosinophilia, often of Helminthic Origin.] *Schweiz. med. Woch*, 1945, Feb. 24, v. 75, No. 8, 165-70. [34 refs.]

[This is a very intriguing article (using the adjective in its journalistic sense) for it is interesting, plausible, and may contain much truth. The author states the problem fairly and marshals his facts and arguments in an orderly fashion.] He starts by giving the characteristic clinical manifestations of Loeffler's syndrome: its benign character and its transitoriness, the slight systemic disturbance, little if any rise of temperature, slight cough, almost total absence of expectoration, and lack of physical signs. He next mentions the X-ray manifestations and the blood-changes, the chief part is devoted to a discussion of the diagnosis and possible aetiology, particularly a bronchio-pneumonia, primary or post-influenzal, epituberculosis (but this is not transient, leaves a permanent scar and is not associated with eosinophilia) and atelectasis. The author then discusses the *ascaridosis* theory and allergy. Loeffler, when bringing his cases before the Swiss Tuberculosis Association in 1936, suggested that the condition might be a "pulmonary tuberculide", a benign tuberculosis, but children and adults presenting the syndrome reacted negatively to the von Pirquet test and the infiltration did not proceed to true tuberculosis. Allergy was postulated to the sun's rays (WIELAND), to cold (LEITNER, and others), to various pollens, privet, lilies, cherry-laurel. MÜLLER, who himself suffered from the syndrome, attributed it to eating raw salads and brought on a recurrence by ingesting soil from his garden which contained *Ascaris* ova, and produced

the same effects in two of his fellow-workers. Thus *Ascaris* could experimentally set up the symptoms, but was it the only cause, and if so, how did it act? *Echinococcus* and *Fasciola hepatica* can produce some of the symptoms, but they cause pain in the liver, rise of temperature, dyspnoea.

Then came the work of VOGEL and MINKING who conducted systematic experiments with *Ascaris*. To six persons they gave *Ascaris* eggs, 6 to 45 in number. In five of these Loeffler's syndrome was produced and in four the worm was found later in the intestines. They made the following observations: The clinical and radiological signs of the syndrome appeared between the 6th and 12th days after infestation and lasted for three to eight days, the radiological opacities "appeared, developed and disappeared" between the 6th and 20th days after infestation, there was sometimes headache, with a sense of fatigue and heaviness of the limbs for 3-4 days; there was cough but no oppression in the chest, fever to 38.4°C. in one patient only; expectoration showed 80 per cent of the cells to be eosinophiles; no *Ascaris* larvae were seen; blood eosinophilia ranged between 8 and 60 per cent. at its maximum from the 19th to the 21st days after infestation. There was observed also, at the time when the pulmonary signs disappeared urticaria, discrete erythema, prurigo and dyshidrosis. Another fact noticed was that ova began to appear in the stools on the 68th day. This means that if we are to attribute the syndrome to *Ascaris* (eggs or larvae) we should look for ova in the stools between nine and ten weeks later. In other words it is not the intestinal parasitism at the time which is the cause of the syndrome, and to prescribe an anthelmintic at the time of the syndrome is to deprive ourselves of an important source of confirmation later (i.e. by finding ova 9-10 weeks afterwards).

It has been thought that the pulmonary manifestations were due to the presence and passage of *Ascaris* larvae in the course of their development and life-history, but larvae are not seen in the sputum nor found in the lungs at autopsy. This is not to be wondered at, for the larvae do not come there to be eliminated in the sputum, but are "birds of passage" passing through the lungs as a stage in their normal development. The interstitial infiltration, the giant cells (foreign body type), the minute haemorrhages are more readily understood as mechanical rather than anaphylactic results of the presence of the larvae, moreover, the syndrome is not produced by intradermal injection of *Ascaris* antigen. In short, the syndrome, it is concluded, is pulmonary ascariidosis and this should be regarded as a "presumptive diagnosis" which can be confirmed by finding ova in the stools 9-10 weeks later, and inquiry should be made as to the patient's having eaten raw salads within the previous ten days [but few could deny this whether they presented the signs of Loeffler's syndrome or not].

H. Harold Scott.

LYON, E & KLEINHAUS, E M. An Eosinophilic Disease with Cutaneous Manifestations associated with Transitory Pulmonary Infiltrations (Loeffler's Syndrome). *Acta Med Orientalia (Palestine & Near East Med. J.)* 1945, May, v 4, No. 5, 144-9, 4 figs

Twenty cases are mentioned as instances of Loeffler's syndrome and two are detailed, one a man of 43 years, the other a woman of 39. There was transitory pulmonary infiltration with eosinophilia, but the symptoms in other respects differed considerably from those regarded as characterizing Loeffler's syndrome. Thus, there was cutaneous oedema with redness of the skin, "resembling urticaria or erysipelas" and a swelling of the roof of the mouth lasting for three days, in one patient. In the other there was localized swelling on the right thigh as large as the palm, a return of the same a fortnight afterwards, and a swelling of the back with pain which persisted for over a month;

also a rise of temperature on the first and third occasions; no mention is made of any rise on the second, nor subsequently when a patch again appeared on the thigh. In the first patient there was also a maculo-papular rash followed four days later by a diffuse tender swelling on the neck. Examination of the stools revealed no helminths or their ova. No statement is made in this respect in any of the other cases. [Obviously, these cases differed in many important respects from what has been reported elsewhere as Loeffler's syndrome.]

H. Harold Scott.

WRIGHT, D. O. & GOLD, E. M. Loeffler's Syndrome associated with Creeping Eruption (Cutaneous Helminthiasis). *J. Amer. Med. Ass.* 1945, Aug. 11, v. 128, No. 15, 1082-3. Refs in footnotes.

During a period of twelve months the authors saw 12 cases of creeping eruption and observed fifteen of them continuously for a fortnight or more, taking X-ray photographs of the chest every three days. Nine of them presented the typical signs of Loeffler's syndrome—patchy migratory infiltration of the lungs, very little, if anything, in the way of physical signs, cyanosis or dyspnoea, and no fever, but with eosinophilia of the blood and sputum. These indicate, as others have also maintained, that the infiltration affects the interstitial tissue of the lungs, predominantly at least.

Total blood counts are not given, but the eosinophil percentage was up to 38 in the blood and to 90 in the sputum. Larvae of *Ancylostoma braziliense* are thought to be the cause in these cases, but no ova or worms were seen in 81 stools examined from the 26 patients. Infestation of the intestine by this nematode is known to be rare.

The Loeffler syndrome has now been reported in association with asthma, pollinosis, undulant fever, tuberculosis, amoebiasis and various helminthic infestations, *Ascaris*, *Trichinella* and others, and with acariasis. "Such a diversified list of etiologic factors lends credence to the view that Loeffler's syndrome is an allergic phenomenon," say the authors.

H. Harold Scott.

GOTSHALK, H. C. Transient Pulmonary Infiltrations (Loeffler's Syndrome). Report of a Case. *Hawaii Med. J.* 1943, July-Aug., v. 4, No. 6, 302-4, 8 figs.

EARLE, K. V. Vincent's Infection in Northern Peru. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1945, Sept., v. 39, No. 1, 77-82. [18 refs.]

Ulcerative stomatitis associated with Vincent's organisms is widespread in the desert region of northern Peru, it is commonest in the *peon* [labouring] class but occurs also in the *empleado* [better paid employee?] class. Among 403 patients admitted to hospital for various complaints, 241 had dental caries, 207 pyorrhoea, and 142 gingivitis. Swabs were taken from the mouths of 63 patients and Vincent's organisms were found in 54, these 54 patients were studied with regard to the presence of avitaminosis and debilitating diseases.

Avitaminosis A was indicated by Bitot's spots (2 cases), nyctalopia (7), phrynoderma (7), fine scaling (17), respiratory disorders (12), and enlarged and septic tonsils (24).

Thiamin deficiency was shown by various signs of neuritis (20), anorexia (10) and constipation (10). Evidence of ariboflavinosis was presented by cheilosis (5), scrotal dermatitis (1) and seborrhoeic disorders. Other probable signs of lack of vitamin B were coarse scaling of the skin (in 1.5 per cent.), hyperpigmented skin areas (34.47 per cent.) and hypopigmented skin areas (20.59 per cent.). Tongue changes included dryness and atrophy (3 cases), magenta colour (2), rawness, soreness, fissures and redness (7).

There were also dental changes which suggested avitaminosis. Debilitating conditions were caused by a variety of diseases.

The author remarks on the absence of tropical ulcer although many conditions thought to be aetiologically related to it were present, and suggests that the temperate and dry climate may be the reason; a table of meteorological readings is given to show the difference of this climate from that of Trinidad, where tropical ulcer is common

J. F. Corson.

SHARP, H. S. & BIGGS, R. A Case of Rhinosporidiosis. *J. Laryngol. & Otol.* 1944, Dec., v. 59, No. 12, 457-8, 1 pl.

An Indian man, a native of Orissa, India, began to get nasal obstruction on the right side in 1933; he came to England in 1937 and, as the obstruction got worse, he attended a hospital in 1938 and had "polypi" removed. Since then he had had nine intranasal operations for recurrent polypi, the longest period of relief being 6 months. He was seen by the authors at Oxford in November 1944.

His right nostril showed several bleeding polypoid growths like pale granulation tissue, on which could be seen several small white spots; there was a thin muco-purulent discharge. The growths were sessile on the septum just in front of the middle and inferior turbinates. They were removed by snare under local anaesthesia with galvanocautery to the base.

The tissue removed had the typical appearance and structure of the polypi caused by *Rhinosporidium seberi*, large numbers of the parasite, in different stages of development, being present in the granulation tissue (see ASHWORTH, this Bulletin, 1923, v. 20, 451; KARUNARATNE, *ibid.*, 1936, v. 33, 720).

J. F. Corson.

GENERAL ENTOMOLOGY

LEWIS, D. J. Observations on the Distribution and Taxonomy of Culicidae (Diptera) in the Sudan. *Trans Roy Entom Soc London*. 1945, June 30, v. 95, Pt 1, 1-24, 2 maps [22 refs]

The paper is a summary of our knowledge of the mosquitoes of the Sudan. The total number of species now known to occur is 127, including 26 anophelines. The map shows that specimens have been collected from almost all parts of the territory, including isolated mountains and oases in the west; the more fertile south-west has apparently not been very fully studied.

The author calls attention to several interesting points in zoogeography. It has been known for some years that the range of certain Mediterranean mosquitoes extends down the Red Sea unto the arid Somali coast, but it now appears that some of these northerners also extend their range much farther west, even to Darfur. Many of the geographical distributions are remarkably discontinuous, and mosquitoes are recorded from certain remote areas surrounded by desert for instance *Anopheles cinereus* is found in Jebel Marra, and *Aedes caspius* in that very isolated spot the Merga oasis. Isolated and discontinuous range such as this (and other examples which might be quoted from the Sahara) are probably due to a much more continuous distribution in a former more rainy epoch.

Among insects of medical interest one observes that *Anopheles gambiae* is found all along the Nile throughout its course through the Sudan, and more widely in the southern and central Sudan. *Anopheles funestus* occurs along

the larger rivers, northwards to about 13°N. also in the Nuba mountains; the distribution of this species and the closely similar *A. rivulorum* and *macmahoni* is shown on a map. *Aedes aegypti* has a very wide distribution, and on the coast is generally represented by a variety in which the normally black areas of the thorax are brown or creamy, though the sharply contrasted black and silver legs remain as in the type. It is a matter of interest that *Culex andersoni*, not otherwise known to occur in the Sudan, has been collected in Khartoum in aircraft coming from Asmara and from Addis Ababa. *A. gambiae* has been found in a train arriving at Port Sudan. P. A. Buxton.

CAMBOURNAC, F. J. C. Culicidae (Diptera, Nematocera) da região de Aguas de Moura. [The Culicidae of the Region of Aguas de Moura.] *An. Inst. Med. Trop. Lisbon.* 1944, Dec., v. 1, No. 2, 247-63, 2 pls. [18 refs.]

THEODOR, O. H. & PARSONS, B. T. Insectary Rearing of *Anopheles pharoensis*. *Bull. Entom. Res.* 1945, July, v. 36, Pt. 1, 79-83.

A colony of *Anopheles pharoensis* was maintained for three generations in the neighbourhood of Cairo between September 1943 and January 1944. This paper describes the methods employed and the results achieved.

The breeding cage was adapted from that described by HACKETT & BATES at the Amsterdam malaria congress in 1933 [see *Rev. Applied Entom.*, Ser. B, 1940, v. 28, 84]. The mosquitoes were fed on sugar and water solution in a small sponge suspended from the cage ceiling; blood meals were obtained from a rabbit at first, subsequently human blood was provided by putting the forearm into the cage once a day. A constant temperature could not be maintained; humidity was provided by a damp blanket; light entered through the glass top and each evening a blue "swarming light" was switched on. Eggs laid in Nile water in Petri dishes were removed daily to white enamel bowls. After some experimentation, first-stage larvae were fed on a suspension of bakers' yeast; from second stage onwards they were fed on finely ground army biscuit. Larvae were exposed to the sun daily for about eight hours. Mean monthly temperatures in the insectary gradually fell from 28.5°C. in September to 13.7°C. in January. On the approach of colder nights attempts to raise the temperature by means of an oil stove failed, mainly because the stove could not be left burning all night. Larvae were therefore kept in an incubator overnight, first at 23°C. and later at 27°C. The duration of the larval period at these temperatures (nightly) was twenty-three and eighteen days respectively. The pupal period was 3-4 days at 20°C. The resulting larvae, pupae and adults were as big and vigorous as in natural habitats.

The colony was started with mosquitoes bred from locally collected larvae and 260 adults were introduced on 31st October to stimulate swarming. By 22nd November 1,033 males and 1,106 females were produced. From this time till 31st January 1,126 males and 1,081 females were entirely laboratory bred. The last batch of eggs was laid on 19th January. The authors believe that with better facilities for maintaining a suitable temperature in the insectary during the cold weather, these figures could be much improved and it was only the lack of these facilities that ended the experiment. H. S. Leeson.

DE MEILLON, B., GOLBERG, L. & LAVOPIERRE, M. The Nutrition of the Larva of *Aedes aegypti* L. I. *J. Exper. Biol.* 1945, Aug., v. 21, Nos. 3 & 4, 84-9.

GOLBERG, L., DE MEILLON, B. & LAVOPIERRE, M. The Nutrition of the Larva of *Aedes aegypti* L. II. Essential Water-Soluble Factors from Yeast. *J. Exper. Biol.* 1945, Aug., v. 21, Nos. 3 & 4, 90-96. [20 refs.]

DE MEIRA, M. T. V. & FERREIRA, T. G. Espèces de phlébotomes de Lisbonne et de ses environs. [Species of *Phlebotomus* in and around Lisbon.] *An. Inst. Med. Trop. Lisbon.* 1944, Dec., v. 1, No. 2, 269-88, 5 pls. (1 map) & 2 figs. English summary. [31 refs]

FERREIRA, F. da C. & FERREIRA, T. Sobre a biologia das espécies de *Phlebotomus* de Lisboa e Arredores. [The Biology of the *Phlebotomus* Species of Lisbon.] *An. Inst. Med. Trop. Lisbon.* 1944, Dec., v. 1, No. 2, 289-313, 5 figs & 1 pl. [41 refs] English summary

BROWN, E. H. Screwworm Infestation in the Nasal Passages and Paranasal Sinuses. *Laryngoscope* 1945, July, v. 55, No. 7, 371-4 [10 refs]

LINDQUIST, A. W., SCHROEDER, H. O. & KNIPLING, E. F. Concentrated Insecticides: Preliminary Studies of the Use of Concentrated Sprays against Houseflies and Mosquitoes. *Soap*. New York. 1945, July, v. 21, No. 7, 109, 111, 113 & 119

This paper sets out primarily to answer the question "would 1 ml. of a fly spray containing 10 per cent. of toxic ingredients be as effective as 10 ml. of spray containing 1 per cent. of toxic ingredients, provided that the concentrated sprays were efficiently atomized?" The authors conclude that this would in fact be the case.

Two insects, the house fly *Musca domestica* and the mosquito *Anopheles quadrimaculatus*, were used in the tests. The insects were exposed in cages which were carried through the treated rooms. The mosquitoes were exposed for one minute and the house flies for five minutes. Pyrethrins and 2,2 bis (parachlor phenyl) 1,1,1 trichloroethane (DDT) were employed as the toxic agents, while the solvent was kerosene supplemented when necessary by some more effective ingredient (unnamed). The concentrated sprays were also compared with dichlorodifluoromethane (Freon-12) aerosols, using equivalent dosages of toxic ingredients in the air space.

From the point of view of economy of solvent and transport, concentrated sprays have obvious advantages. When finely atomized as with a De Vilbiss paint spray gun operated at 25 lb. per sq. in., equal quantities of DDT, or pyrethrins, or mixtures of the two, gave similar knockdowns and kills, whether dispersed from concentrated (e.g. 16 per cent. DDT) or dilute (e.g. 1 per cent. DDT) solutions. These concentrated, finely dispersed sprays also compared favourably with Freon aerosols when tested biologically. When houseflies were exposed in rooms treated with 4 mgm. pyrethrins and 40 mgm. DDT per 1,000 cu. ft. for five minutes, and the exposure was commenced even thirty minutes after spraying, kills in the region of 85-95 per cent. resulted from both the aerosol and concentrated spray applications. In the latter case the spray was applied by a pocket-size capillary-tube sprayer specially designed to distribute these concentrated sprays. In practical terms such a sprayer, if it contained 75 ml. of concentrated spray, would be capable of treating 150,000 cu. ft. of space, which would require approximately 2½ quarts of "Official Test Insecticide" (0.1 per cent. w/v pyrethrins) if finely atomized, or about one gallon if dispersed through an ordinary hand sprayer. W. A. L. David.

STARR, D. F. Use of a Double-Nozzled Spray Apparatus for the Application of DDT or Oils. *Science*. 1945, Aug. 10, 156-7.

By mixing two sprays, one of DDT solution and the other of water, a deposit on the sprayed surface was obtained which was superior in quantity and quality to that obtained by using a spray of DDT solution alone. The DDT

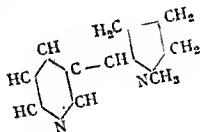
on was sprayed from a small atomizer and the water spray was from a type paint sprayer. The two nozzles were set to converge at an angle of 90° and the two sprays met at 2 to 4 cm. from the nozzles. When the DDT solution was made with water-miscible solvents such as acetone, dioxane or alcohol, the DDT was deposited as "nascent precipitates," the liquid and some solid; when solvents not miscible with water, such as kerosene, were used, the solvent (oil) remained on the sprayed surface while the water drained off and a heavy deposit of oil could be obtained without losing much of the water draining off. The deposits of DDT on glass were extremely resistant to water dropped or poured over them like rain; some nascent deposits showed no decrease in amount after 7 hours of such treatment. Oranges and apples were successfully sprayed by this method.

J. F. Corson.

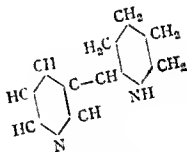
GEAR, H. S. A Note on the Use of D.D.T. in Medical and Health Problems. *South African Med. J.* 1945, Aug 25 v 19, No 16, 290-92

NABOKOV, V. A. Anabesine Sulfate: a Protective Agent against Bites of Malarial Mosquitoes. *Amer. Rev. Soviet Med.* 1945, June, v. 2, No. 5, 449-52.

A useful repellent for mosquitoes was found in the substance anabesine sulphate prepared from the plant *Anabasis aphylla* (Chenopodiaceae). Anabesine, which is the chief alkaloid present (55 per cent. of total alkaloids), has a formula somewhat similar to nicotine, thus —



Nicotine



Anabesine

Anabasis is common in the U.S.S.R. and the alkaloids in the form of sulphates have been widely used as insecticides. Undiluted anabesine sulphate is a dark brown, oily liquid with a characteristic irritating odour. It is soluble in water and alcohol, giving an acid reaction. The 5 per cent. solution is almost odourless and can be wiped off the skin without difficulty.

Aqueous solutions of 1, 3, 5 and 10 per cent. were tested for mosquito repellent powers. It was found that none of them greatly diminished the numbers of mosquitoes alighting and that 1 and 3 per cent. had no effect in preventing bites. However, with 5 per cent. and still more with 10 per cent., there was a very high degree of protection from bites. This protection lasts for five to six hours and with two applications complete protection is ensured for ten to eleven hours.

The possibility of dermatitis was investigated by patch tests. A 50 per cent. alcoholic or aqueous solution applied for four days gave some reaction (erythema with minute follicular nodules) but the application of 5 per cent. solution twice daily for a month to face, neck, chest and arms did not produce any harmful effect on the author.

Anabesine, like nicotine, can be absorbed through intact skin and can produce systemic toxicity. It is, however, considerably less toxic than nicotine; 0.1 mgm. of nicotine being equal to 0.5 mgm. anabesine or 1 mgm. lobeline. Anabesine sulphate is much less toxic than the base and should not be dangerous when used diluted.

J. R. Busvine.

LABORATORY AND TECHNICAL PROCEDURES.

GILLMAN, T. & GILLMAN, J., with the technical assistance of J. G. BRYDEN. *A Modified Liver Aspiration Biopsy Apparatus and Technique*, with special reference to its Clinical Applications as assessed by 500 Biopsies. *South African J. Med. Sci.* 1945, June, v 10, No. 2, 53-66, 1 text fig. & 5 figs. on 1 pl. [26 refs.]

The operation of liver puncture has not hitherto been free from danger to life, as from 1 to 2 per cent of patients have been killed by it, usually from haemorrhage due to tearing of the liver tissue by the needle. In a proportion (22.5 and 50 per cent) of cases, also, the operation has failed, liver tissue not having been obtained.

The authors have modified the syringe and needle of IVERSEN and ROHOLM (*Acta Med. Scandinavica*, 1939, v 102, 1) in several particulars: the stylet remains in the cannula, so preventing the liver tissue from being drawn into the syringe; the back of the plunger has a rubber buffer; the end of the cannula is bevelled and makes a slit wound instead of a gaping round hole in the liver; the shaft of the plunger is locked in position when the plunger is pulled back, so preventing the tissue in the cannula from being accidentally expelled by recoil of the plunger.

Patients fast for 12 hours before the operation. If the liver is enlarged or if there is jaundice the prothrombin level is determined and vitamin K given if required. Morphine is only necessary in very nervous patients or if the liver is very tender.

If the liver is much enlarged the patient lies flat in bed with arms extended above his head; in other cases he is propped up in a semi-sitting position. Babies are dealt with in the semi-sitting position.

The skin and underlying tissues (including the peritoneum) in the apex of the angle between the xiphisternum and the right costal margin, are successively anaesthetized with 2 per cent novocain, in a direction slightly upward and to the left. Anaesthesia is established in 2-3 minutes, then the skin is slightly incised and the needle, attached to the syringe, is pushed upwards, backwards, and slightly to the left until the surface of the liver is felt, when the "depthguard" is quickly adjusted to permit the needle to go only 2-3 cm. further. The needle is pushed into the liver and the plunger quickly withdrawn, and the barrel quickly twisted through 360 degrees on the plunger and the instrument withdrawn. The whole operation of puncture should take less than 15 seconds.

The method was tested first on baboons and human corpses and has since been used in more than 500 biopsies on 260 human subjects and in more than 150 on baboons and other monkeys, without shock or haemorrhage, and in more than one death; in that case haemorrhage was due to puncture of an unusual artery in the liver and not to tearing of liver tissue. The authors have used

it in normal subjects (20), cases of pellagra (92 infants and 349 adults), carcinoma of the liver (16), cirrhosis of the liver (10), hepatitis, tuberculosis, schistosomiasis, malaria and diabetes. In diffuse lesions it is reliable, but in localized lesions positive results only are significant.

The authors refer to their results (some still in the press) and to the work of ROHLM and IVERSEN (*Acta Path. Microbiol. Scandinavica*, 1939, v. 16, 427) and of DIBLE, McMICHAEL and SHERLOCK (*Bulletin of Hygiene*, 1944, v. 19, 14) and mention other applications of this method of liver puncture. [See *J. F. Corson*. also this *Bulletin*, 1944, v. 41, 1057, 1058.]

SHERLOCK, Sheila. Aspiration Liver Biopsy. Technique and Diagnostic Application. *Lancet*. 1945, Sept. 29, 397-401, 6 figs. [22 refs.]

The technique of aspiration liver biopsy is described and the risks involved and its use in diagnosis are discussed.

A jaundiced patient should be given vitamin K for 3 days before the puncture is made; in non-obstructive jaundice (urobilin in the urine) two 5 mgm. tablets of "Kapillon" should be given by mouth three times a day, while in obstructive jaundice a daily dose of 5 mgm should be injected intramuscularly. The patient's blood group must be known and two pints of compatible blood must be ready for transfusion if required. A sedative before puncture is not necessary.

The patient lies supine in bed with his right side near the edge and his right arm placed behind his head; a firm pillow may be placed under his left side to tilt his body slightly to the right.

The cannula is 15 cm. long and 1 mm. in bore and is fitted with a handled trocar; a 20 cc. "record" syringe is used.

The puncture is made in the mid-axillary or anterior axillary line in the 9th or 10th intercostal space [cf. GILLMAN and GILLMAN, above]. The skin is anaesthetized with 2 per cent. procaine [novocain] solution and by means of a long fine-bore needle the pleura and peritoneum and liver capsule are also anaesthetized, at least 10 cc. of solution being required.

The trocar and cannula are passed through the skin (which may be previously incised) and the patient is told "take a deep breath in, let it out, and then hold your breath." This displaces the lung upwards and ensures apposition of the diaphragmatic and costal pleurae. The trocar and cannula are then pushed into the liver, and when it is fully half an inch within the liver, the trocar is withdrawn and the cannula pushed in for a further 4-5 cm. to punch out a cylinder of liver tissue; the syringe is then attached and suction maintained while the cannula is withdrawn. The puncture wound is sealed with collodion. The liver fragment is usually found in the barrel of the syringe [see GILLMAN & GILLMAN above].

Afterwards a small dose of morphine may be given to relieve pain and in the evening a sedative such as barbitone soluble, 10 grains. The pulse rate should be charted hourly for the first 24 hours and if it rises, the physician should be called. Routine visits should be made 4 and 8 hours after the biopsy. If there is any sign of haemorrhage blood transfusion should be done. Absolute rest in bed for the first 24 hours is essential, but the patient may then get up and leave the hospital 48 hours after the puncture.

Difficulties.—The author and her colleagues [see DIBLE, McMICHAEL and SHERLOCK, *Bulletin of Hygiene*, 1944, v. 19, 14] failed to obtain a suitable specimen of liver tissue in 10 per cent. of their first 126 biopsies but in only 2 per cent. of the next 138. Difficulties arise chiefly in hepatic cirrhosis, especially if ascites is also present; also, in pulmonary emphysema the liver is pushed downwards and the cannula may easily pass above it.

Risks.—Fatality rates in the past varied from 0 to 3 per cent. (a table is given); in the present series of 264 punctures there were two deaths (one patient was already moribund) which occurred in the first 126 cases [see DIBLE *et al. loc. cit.*]. This decrease in risk is due to changes in technique and a more careful selection of cases. The bore of the cannula was reduced from 2 mm. to 1 mm. and the length increased from 10 cm. to 15 cm. which enables the capsule of the liver to be cut cleanly by the trocar. The risk of haemorrhage is greatest in severely jaundiced patients especially in acute parenchymatous liver disease; in the former series (126 cases) haemorrhage occurred in 5 out of 83 cases with jaundice, in the latter (138 cases) in none out of 74.

Except in localized lesions the information obtained by this method is reliable, sections of 10–20 liver lobules can be cut from the piece removed. Diseases in which it is useful for diagnosis are: acute hepatitis, cirrhosis of the liver, obstructive jaundice, malignant disease of the liver, blood diseases, amyloid disease, kala azar, and various other diseases; notes on some cases are given. The method may also be used to test the action of drugs on the liver.

J. F. Corson.

FULLER, A. T. The Estimation of Aromatic Amidines. *Biochem. J.* 1945, v. 39, No. 1, 99–102, 2 figs.

The principle of the estimation is that when solutions of aromatic amidines are heated with glyoxal sodium bisulphite and boric acid at pH 9 a colour (usually magenta) is produced which can be measured in the usual ways. The reaction is specific for an unsubstituted amidine directly joined to an aromatic nucleus, other amidines cannot be measured in this way. Thus the method can be used for stilbamidine, propamidine, and V.187 (*p*-methyl sulphonyl benzamidine), although with the first two of these the method is not sensitive enough to measure therapeutic blood concentrations. The compounds can be estimated in blood, urine, and laetes. The exact instructions for carrying out the estimation vary somewhat with the different compounds, their concentrations and the biological fluid in which they are present; for these technical details, the original paper should be consulted. F. Hawking.

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS.

FAN, J. H. Communicable Diseases in China during Recent Years. *Epidemiological Information Bull.* (UNRRA Health Division), Washington, D.C. 1945, July 31, v. 1, No. 12, 495–536, 1 map. [38 refs.]

This is a detailed summary of reports on the occurrence, during the years 1939–44, of seven of the ten notifiable diseases in China; they are: plague, smallpox, typhus, relapsing fever, cholera, dysentery and typhoid fever (including paratyphoid fevers).

Plague.—During recent years plague has become more prevalent and has spread inland from the south-eastern coastal regions. In 1940 the Japanese dropped rice and wheat mixed with rat-fleas over the city of Chu-hsien and probably over Ning-po, and plague appeared for the first time in these cities soon afterwards and is thought to have been caused in this way. There were

11,729 cases of plague in ten provinces during the period, those chiefly affected being Fukien and Chekiang; in the former the incidence rate averaged 16 per 100,000 of the population, and in the latter 23.4 per 100,000.

Smallpox.—Localized outbreaks still occur, especially in connexion with migrations of population, and in 1941 and 1942 there was a widespread epidemic. In 19 provinces 38,836 cases were reported, the average rate of incidence being 2.4 per 100,000 of the population.

Typhus.—In North China, where it is the most prevalent, it corresponds clinically and epidemiologically, according to many authors, to the epidemic type, but murine flea-borne or endemic typhus has been proved to exist in Peiping and was reported from Shanghai. In 19 provinces 23,130 cases were reported, an average incidence of 1.8 per 100,000.

Relapsing fever.—This is louse-borne in China; 72,845 cases were reported in 19 provinces, the average incidence being 4.7 per 100,000. In certain Chinese armies there were 12.3 cases per 1,000 in 1939 and 7.4 in 1940, among about half a million men in each year.

Cholera.—During the period, 92,216 cases (5.5 per 100,000) were reported in 19 provinces.

Dysentery.—It is estimated that bacillary dysentery formed about 90 per cent. of the total cases reported; there were 361,361 cases (25.9 per 100,000) in 19 provinces. In certain Chinese armies rates of incidence of 12.8 and 8.7 per 1,000 occurred in 1939 and 1940 respectively.

Typhoid fever.—In North China paratyphoid A, B and C fevers are said to be prevalent as well as typhoid fever; 64,097 cases (4.6 per 100,000), including paratyphoid, were reported during the period.

The spread of plague and of some of the other diseases is discussed in some detail and figures of monthly incidence in the counties of the provinces are shown in tables; a map is given and there are 38 references.

J. F. Corson.

WICKRAMASINGHE, W. G. A National Health Service for Ceylon. *J. Ceylon Branch Brit. Med. Ass.* 1945, Apr., v. 41, No. 1, 1-12.

BOOK REVIEWS.

LEE, David J. [B.Sc.] & WOODHILL, A. R. [B.Sc. Agr. (A.A.M.C., Australia)]. *The Anopheline Mosquitoes of the Australasian Region.* Publications of the University of Sydney, Dept. of Zoology. Monograph No. 2, pp. xii + 209, 34 pls., 8 maps & 13 figs. 1944, Glebe, N.S.W.: Australasian Medical Publishing Company Ltd., Seamer Street.

As a result of some two years' collaboration, and with the help of the Mobile Entomological Units, the Malaria Control Units and other members of the Australian Army Medical Corps, the authors have produced this concise review of existing knowledge on the Australasian anophelines. The region covered includes Australia, Tasmania, and islands eastward to 180° longitude; New Guinea and islands northward to the equator, and the Moluccas, Ceram and Timor.

In the introduction, general matters concerning morphology, biology and control are briefly discussed. EDWARDS's classification is followed in all but minor respects; one departure is the adoption of the recent American custom of trinomial nomenclature for subspecies, a practice which the authors discuss in the section on "Systematics".

Special attention is paid to the characters used for the identification of adults and larvae in the account of the external morphology of the tribe *Anophelini* taking *Anopheles annulipes* as the basis for comparison. The main body of the work, comprising some 130 pages, consists of detailed descriptions of the known males, females and larvae of about forty species and varieties; but in only six are eggs described, and pupae in none. There are keys to the species, notes on synonymy, type localities, biology and relation to disease. Closely related species and forms are compared, particularly the *A. punctulatus* complex, which comprises at least two, probably three and possibly more subspecies. The subspecies *punctulatus* and *moluccensis* are the principal dangerous vectors of malaria in the Australasian region; both occur in the Moluccas, New Guinea, New Ireland, the Solomons and other islands, where they form the dominant element of the anopheline population, but *moluccensis* occurs also on the mainland in Northern Australia and Queensland.

In addition, in less detail, short accounts of twelve other anophelines which occur on the western fringe of the Australasian region are appended. Three of them, *A. minimus*, *A. maculatus* and *A. sundanicus*, important vectors of malaria elsewhere, are recorded from Tumor.

Recognition of the main distinguishing characters of the Australasian species and their distribution is greatly assisted by the clear line drawings in plates, text figures and maps. References are given to 120 papers and journals (some of them in the Dutch language) and an index is provided.

This much-needed, up-to-date monograph fills another gap on the library shelves of the medical entomologist, though revision will be required as knowledge increases. The control of mosquitoes does not come within the scope of this publication, but attention is drawn to some of its entomological aspects. Medical officers, malariologists and others will certainly gain much information regarding variations in morphology, biology and habits of these species of *Anopheles*, which will enable them to adapt their control measures to local circumstances.

H. S. LEESON.

TROWELL, H. C. [M.D., F.R.C.P. (Lond.), etc.] *Diagnosis and Treatment of Diseases in the Tropics*. Baillière's Medical Manuals for Africans, 2nd Edition pp. xiv + 219 35 figs. 1945. London: Baillière, Tindall & Cox, 7 & 8 Henrietta Street, Covent Garden, W.C.2. [4s.]

Writing this book must have been an undertaking far from easy. It necessitated a thorough knowledge of the mind of the better educated native African, of his capabilities of absorbing instruction and of applying the knowledge imparted, there was the additional difficulty of deciding what to teach and what to leave out in order to produce a competent dresser and nurse, one able to undertake on emergency even greater responsibilities, but not to overpass this boundary so that the student would come to think that he was able to act as a qualified doctor and assume greater responsibility than his instruction warranted.

This task could not have been entrusted to better hands. The author possesses the highest medical qualifications obtainable, he has been for some years in close touch with East Africans and engaged in instilling into them the elements of medicine and surgery.

The book is clearly intended to supplement lectures and notes and not to replace them. Thus, to give a single example, the instruction to "relieve pain by opium and morphia," or in the case of smallpox to "treat the case by nursing, fluid diet, opium and morphia" is too vague, if no dose or method of administration is mentioned.

There is little to add to what was written by the reviewer of this book when it was first published in 1939 [see this *Bulletin*, 1939, v. 36, 876], for the differences between that and the present issue are small. A few words here and there have been added on the use of one or other of the sulphonamide group of drugs, and a chapter on Diets and Malnutrition. This last was an important omission from the first edition and has now been remedied and the work has been done well. The fact, often forgotten or neglected, that "in disease the body requires just the same amounts of food as in health" recalls the dictum of a bygone physician (was it not Graves?) who wished to have as his epitaph the words "He fed fevers."

Apart from the changes referred to, the new edition seems to be merely a reprint of the old, even the same misprints (very few, it is true) remain and the Index is the same except for the single addition of M. & B. The print is not so clear as in the first issue and the blocks show signs of wear, but these are probably inevitable in a war-time production. There are two or three matters omitted which one would have expected to see, and here and there directions and statements might be more clearly expressed. Thus, under Pneumonia, the danger of heart failure and sudden syncope is not, in the reviewer's opinion, sufficiently indicated. Death in pneumonia is due, in a large majority of cases, to the stress on the heart. To say that "Heart failure . . . should be prevented by resting the patient" is not enough; mere raising in bed or turning unassisted may result in stoppage of a heart whose burden is already almost more than it can bear. On the same subject a question is asked: "What is the usual treatment of pneumonia as regards . . . diet?" Looking up the text for answer all we find is: "The diet is according to the patient's appetite," unless the harassed native student applies the instruction given a few lines above: "The patient must be fed and helped with the bedpan." A similar instance of Horace's *Brevis esse laboro, obscurus fio* occurs on p. 120, where the treatment of intestinal haemorrhage in typhoid fever is given as "stopping all feeding and morphia injection." On p. 61, on the treatment of Sprains, we find: "The sprained joint should not be used much for at least a week or two, possibly for longer," followed immediately by the words "an injection of procaine into the strained ligaments . . . allows the patient to use the affected joint immediately." The administration of sulphaguanidine in dysentery, of gentian violet for threadworm infestations and of mepacrine in malaria shows that the information has been generally brought up to date. On the other hand the use of serum in cerebrospinal fever is not even referred to [has it been entirely superseded?] and though syphilis and syphilitic aortitis are spoken of, aneurysm is omitted from the causes of cough, in spite of its being troublesome and of characteristic type. Of the Cestodes *Taenia saginata* is considered, but nothing is said of *T. solium* or of hydatid. Yaws and gangosa are spoken of, but we find nothing about goundou or juxta-articular nodules, except in the case of the former, the remark that "yaws or syphilis may attack the bones of the nose and the roof of the mouth"; myiasis receives no mention. Smallpox is spoken of, and rightly, as a very serious disease, but there is no reference to alastrim. Droplet infection is explained on p. 134, but elsewhere infection so conveyed is designated "inhalation of sputum." The frequent advice to apply hot fomentations would lead the student to infer that some fomentations are applied cold.

Most of the above remarks deal, it is true, with minor points, but it is these so-called minor points which might have been corrected when the new edition was called for. At the same time they cannot be said to detract from the intrinsic value of a good piece of work which should prove most useful and instructive to those for whom it has been specially written. The East African student is indeed fortunate in having so sound a teacher as Dr. Trowell.

H. Harold Scott.

MEDICAL RESEARCH COUNCIL. *The Medical Use of Sulphonamides.* By various authors. (Edited by F. HAWKING & F. H. K. GREEN). 2nd Edition. M.R.C. War Memorandum No. 10. 71 pp. 1945. London: H.M. Stationery Office. [1s. 3d.]

Over 50,000 copies of the first edition of this Memorandum [*this Bulletin*, 1943, v. 40, 867] have been sold in two years. The new edition, which has increased in length by some 30 pages, retains all the valuable features of the original, but has been considerably amplified in the light of subsequent experience. There are numerous minor additions, but the authors' main task has been to give accounts of new sulphonamide compounds, and to adjust the therapeutic methods recommended to the new situation created by the advent of penicillin. Among the former only "Sulphamerazine," phthalylsulphathiazole and "Marfanil" are described fully, although other new drugs are more briefly mentioned in connexion with the treatment of particular infections. Penicillin is dealt with by a new section on the relation of sulphonamide to penicillin therapy, which outlines their separate spheres and discusses their respective merits for the treatment of many conditions in which these spheres overlap. The stronger indications for penicillin are also emphasized in subsequent sections treating of individual infections and diseases, but its dosage and the technique of administration are not discussed. The first edition was written as a guide to the use of sulphonamides "in the light of their present or potential availability in Great Britain." The supply position for most sulphonamides has greatly improved, but the "availability" of penicillin presents far more serious problems than that of, say, sulphathiazole two years ago, and the authors have therefore been commendably cautious, retaining full instructions for sulphonamide treatment even in conditions in which penicillin is the treatment of choice. There are extensive sections on the treatment of wounds and burns, and an interesting discussion of group prophylaxis as applied to cerebrospinal fever, dysentery, and streptococcal infections of the upper air passages. As before, numerous references, mainly to recent work, are given in the text. The influence of this publication in rationalizing sulphonamide treatment must already have been very great, and the present edition should maintain and extend it.

L. P. Garrod.

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ERRATA.

In lines 1 and 2 of the abstract of CARMICHAEL and BELL's paper on a new phenanthridinium compound (1553) in this *Bulletin*, 1945, v. 42, 260, the group "9-phenyl" was inadvertently omitted from the formula which should read 2·7-diamino-9-phenyl-10-methylphenanthridinium bromide.

In the title of the paper by EAGLE abstracted in this *Bulletin*, 1945, v. 42, 354, the Greek letter *gamma* was misprinted as V, the name of the drug should read γ -(p-Arsenosphenyl)-Butyric Acid.

In the abstract of Dr. A. F. FOWLER's paper in this *Bulletin*, 1945, v. 42, 541, the sentence "Trypanosomes were present in the cerebrospinal fluid in 33 of the 42 patients" should read, as explained by the author in his paper "Positive C.S.F. means that there was either direct or indirect evidence of central nervous system involvement. Thus thirty-three cases, i.e., 78 per cent. showed involvement of the central nervous system". The abstracter regrets to have overlooked this explanation of the + sign in the table

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(The bracketed abbreviations after the page numbers indicate the subjects.
Page numbers within brackets indicate papers not summarized.)

Am. signifies	Amoebiasis and Intestinal Protozoal Infections.	Lep. signifies	Leprosy.
Bart.	" Bartonellosis.	Mal.	" Malaria.
Bl.	" Blackwater.	Misc	" Miscellaneous.
B.R.	" Book Review	Misc Dis	" Miscellaneous Diseases.
Chl.	" Cholera.	Oph.	" Tropical Ophthalmology.
Def. Dis.	" Deficiency Diseases including Epidemic Dropsy	Pl.	" Plague.
Den.	" Dengue and Sandfly Fever.	Prot.	" General Protozoology.
Der.	" Dermatology and Fungous Diseases	Rab	" Rabies.
Dys.	" Dysentery (Bacillary and Unclassed).	R.F.	" Relapsing Fever and other Spirochaetoses.
Ent.	" General Entomology	Reports, etc.	" Reports, Surveys and Miscellaneous Papers.
Haem.	" Haematology.	Sp.	" Sprue
Heat Str.	" Heat Stroke and Allied Conditions.	Tryp	" Trypanosomiasis.
Hel.	" Helminthiasis	Typh.	" Fevers of the Typhus Group
Lab.	" Laboratory Procedures.	Ulc.	" Tropical Ulcer
Leish.	" Leishmaniasis.	Vms.	" Venoms and Antivenenes.
		Y.F.	" Yellow Fever
		Ys.	" Yaws.

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 erberg, E. J., with Gordon, (940) (Ent)
 erman, W. M., 819 (Hel.)
 —, with McGavack, 141 (Haem)
 etting, V. A., (662) (Ent.)
 hahoungul, P., 57 (Def. Dis.)
 hosh, J. K., with Bose, 207 (Dys)
 —, with — & Rakshit, 444 (Mal.), 468 (Am.)
 hosh, T. K., (65) (Vms)
 li Giacomo, M. P. & Mayer, R. A., 47 (Hel)
 ibson, T. E., 396 (Hel)
 ilsen, H. K., 906 (Hel.)
 Giglioli, G., 815 (Mal.)
 Gilbert, W., 490 (Oph)
 Gilbertson, W. E., 641 (Den)
 Gilchrist, M., with King, 781, 782 (Mal)
 Gifford, G. H., 487 (Oph.)
 Gill, C. A., 282 (Chl.)
 Gill, D., with Brugsch, 141 (Haem)
 Gillman, J., with Gillman, 748 (Def. Dis.), 1046 (Lab)
 Gillman, T. & Gillman, J., 748 (Def. Dis.), 1046 (Lab)
 Gillet, F., with Sarrouy, 101 (Leish)
 —, with —, Dendale, Combe & Arnaud, 102 (Leish.)
 Gilroy, A. B. & Ghwatt, L. J., 786 (Mal)
 Ginsburg, J. M., 939 (Ent)
 Gintscheff, P. Z., 882 (Typh)
 Giordano, A. F., 37 (Am.)
 Girard, G., 375, 377 (Pl)
 Giroud, P., 199, 366 bis, (Typh.)
 — & Panthier, R., 104, 935 (Typh)
 Giusti, G. L., with Segura, Radice & Donin (141) (Haem.)
 Gullin, G. M., with Knipling & Yates, 73 (Ent)
 Glasgow, R. D. & Blair, R., 4 (Mal)
 Glass, W. W., Jr., with Gordon, Lippincott, Marble, Ball & Ellerbrook, 692 (Mal)
 Glauser, F., 479 (Hel.)
 Gloeckner, A., with Kessel, Allison, Kaime & Quiros, 40 (Am.)
 Góbiros, E., with Rivas & Mantilla, 910 bis (Hel.)

van Goidensenhoven, C., with Rodham, 869 (Tryp.)
 — & Schoenaers, F., 791 (Tryp.)
 Gulberg, L., de Meillon, B. & Lavoipierre, M., (1043) (Ent.)
 —, with — & — (1043) (Ent.)
 Gold, E. M., with Wright, 1041 (Misc. Dis)
 Goldblum, N., with Birnbaum & Kligler, 700 (Bl)
 Golden, A., 718 (Typh)
 Goldman, L., 480 (Hel.), 843 (Ent.)
 Gontacava, A. A., with Beklemishev, 248 (Mal)
 González Q. J., with Del Pozo & Anguiano, 653 (Vms)
 González Ochoa, A. & Ruiloba, J., 142 (Der.)
 Gonzalez Peris, G., with Trespacios & de Laosa, 586 (Der)
 Gonzalez Prendes, M. A., with Ibarra Perez, (214), 1009 (Lep)
 González Ureña, J., (1010) (Lep)
 Goobar, J. K., with Savino, 33, 466 (Pl)
 Good, R., 91 (Mal)
 Goodwin, L. G., 262 (Leish.)
 Goodwin, M., with Mulrennan & Shannon, 633 (Mal)
 Gordon, H. H., Lippincott, S. W., Marble, A., Ball, A. L., Ellerbrook, L. D. & Glass, W. W., Jr., 692 (Mal)
 Gordon, R. M., 255 (Mal)
 — & Davey, T. H., 541 (Bl.)
 —, with Hill, 940 (Ent)
 Gordon, W. M. & Gerberg, E. J., (940) (Ent.)
 Goracheva, L. K., 575 (Hel)
 Gorss, P. & Accart, R., 395 (Hel.)
 Gotshalk, H. C., (1041) (Misc. Dis)
 Gottfried, S. P., 885 (Typh.)
 Gouck, H. K., with Smith, 151 (Ent.)
 Gouvêa, L., with Magalhães, Coutinho & Ignacio, 1016 (Hel)
 Grabar, P., with Gallut, 807 (Chl)
 Graham, J. G. & Naftalin, J. M., 876 (Leish.)
 Di Grandi, J., with von Sallmann & Meyer, 489 (Oph.)
 Grant, G. H., with Apley, 836 (Misc. Dis)
 Grant, J., Anderson, M. & Thompson, R. B., 187 (Tryp)
 Grasset, E., 829 (Vms)
 Grau, M. L., 232 (Lab)
 Grau Triana, J., 212 (Lep.)
 —, de Castro Palomino, J. & Conde Mateo, E., 213 (Lep)
 Gray, W. A., with Anderson, von Deschwanden & Menzies, 961 (Mal.)
 Green, G. E., with Bercovitz, Rodriguez-Molina, Hargrave & Dickie, 47 (Hel)
 Green, F. H. K., with Hawking, 1052 (B.R.)
 Green, R. A., 442 (Mal)
 Greenburg, N., with Heilman & Knutson, 893 bis (R.F.)
 Greenslade, G. M. & Morrison, D. (229) (Prot)
 Greiff, D., Pinkerton, H. & Moragues, V., 362 (Typh.)
 Grieco, S. J., with Galvão & Corrêa, 4 (Mal)
 Griffiths, J. J., 284 (Chl.)
 Grindley, D. N., with Henry, 783 (Mal.)
 Grunmashevsky, L. V., Bagrova, A. S. & Stepanov, I. R., 460 (Typh)
 — & Stepanov, I. R., 191 (Typh.)

- Groszler & Lefèvre, (1038) (Misc. Dis)
 Gruber, C. M., with Potter & Bronstein, 690 (Mal)
 Guasch, J., 426 (B.R.)
 Guerra, F., Beltrán, E., De la Garza, F. & Raúl Larena, M., 866 (Mal)
 Guggenheim, K., with Jügler & Schwartz, 930 (Heat Str.)
 Guhl, R., 51 (Hel)
 Guimarães, F. N., 812 (Ys)
 —, with da Cunha, Leão & Cardoso, 1003 (Ys)
 Gulamova, V. P., with Vamberg, Perekhostova & Ostrovskaya, 549 (Typh.)
 Gunther, C. E. M., 849 (B.R.)
 Gupta, J. C., & Ganguly, S. C., 943 (Reports, etc.)
 — & Kahali, B. S., 191 (Leish)
 —, with Pal, Mukerji & Chatterjee, 286 (Am)
 Gupta, L. M., with Ransome & Patterson, 146 (Misc. Dis)
 Gupta, R. D. & Laha, P. N., 87 (Mal)
 Gumann, M. J., 1031 (Oph.)
 Guttschich, A. V., 533 (Mal)
 Güter, O. K. G., with Manson-Bahr, 409 (Misc. Dis)

H.

- Haa, E., 282 (Mal)
 Haas, V. H. & Ewing, F. M., 539 (Mal)
 —, Feldman, H. A. & Ewing, F. M., 865 (Mal)
 Hackett, C. J., 255 (Mal)
 Hadaway, A. B., with Symes, 785 (Mal)
 Haddow, A. J., with Smithburn, 320 (Misc. Dis)
 —, with — & Mahaffy, 321 (Misc. Dis)
 Haide, G. L., with Skipper, 451 (Bl.)
 Halbesen, W. A., with Stryker & Leventhal, 581 (Def. Dis)
 Hall, J. E., with Butt, Watkins & Cragg, 783 (Mal)
 Hall, S. A., Schechter, M. S. & Fleck, E. I., 842 (Ent)
 Hall, T. F., with Hess, 626 (Mal)
 Hallervorden, J., 638 (Typh.)
 Halpert, B. & Ashley, J. D., Jr., 126 (Am)
 Hamblen, H. L., Piott, H. & Smadel, J. E., 796 (Typh.)
 Hamilton, T. R., with Angevine, Wallace & Hazard, 976 (Leish)
 Hamon, W. G. & Ouary, G., 495 (Ule)
 Hamzick, D. L. & Chambers, W. E., (349) (Mal)
 — & Frith, D. S. (Mal)
 Hammond, A. G., 1038 (Ulc)
 Hamre, D., with Jones & Baker, 543 (Leish)
 Hanschell, H. M., 845 (Reports, etc.)
 Hanzlik, P. J., with Dreisbach, 864 (Mal)
 Hardenbergh, W. A., (229) (Ent)
 Hardesty, J. F., 1038 (Oph)
 Hardin, R. D. & Hawking, F., 188 (Tryp)
 Hardwick, S. W., 926 (Def. Dis)
 Hardy, J. D. & Passmore, R., (877) (Leish)
 Hargitt, M. V., 558 (Y.F.)
 — & Burruss, H. W., 803 (Y.F.)

- Hargrave, D. W., with Bercovitz, Rodriguez-Molina, Dickie & Green, 47 (Hel)
 Hargreaves, W. H., 558, 895 (Am)
 —, with Duxon, 907 (Hel)
 Harrington, C. & Young, E. A. E., 271 (Typh.)
 Harned, B. K. & Etteldorf, J. N., 443 (Mal)
 Harper, A. R., (1027) (Der)
 Harper, J. G. M., with Almy, 646, 815 (Hel)
 Harper, J. O., with Garnham, 447 (Mal)
 Harrell, G. T. & Horne, S. F., (926) (Hel)
 —, with —, 306 (Hel)
 —, Venning, W. & Wolf, W. A., 373 (Typh.)
 —, Wolf, W. A. & Venning, W., 888 (Typh.)
 Harris, P. N., 595 (Reports, etc.)
 Harrison, H. E., Tompsett, R. R. & Barr, D. P., 222 (Sp)
 Harrison, I., with Cohen, 643 (Am)
 Harrison, K. S. & Dakin, W. P. H., 178 (Mal)
 Hart, V. L., 211 (R.F.)
 Hartz, H., with van der Sar, 837 (Misc. Dis)
 Hartz, P. H., 480 (Hel), 592 (Misc. Dis)
 Harvey, A., with David & Brace, 229 (Ent)
 Harvey, A. M., 963 (Mal)
 Hasche-Kjünder, R., 167 (Rab)
 Hatch, W. E. & Wells, A. H., 312 (Der)
 Hauser, A. & Deckert, K., 809 (Am)
 Havard, R. E., with Macgrath, 12 (Bl.), 863 (Mal)
 —, with —, Brown, Rositer, Irvine, Lees, Parsons, Partington & Rennie, 251 (Mal)
 —, with — & Parsons, 568 (Bl)
 Hawking, F., 538 (Mal), 871 (Tryp)
 — & Green, F. H. K., 1052 (B.R.)
 —, with Harding, 188 (Tryp)
 Hawkins, P. A. & Cole, C. L., 812 (Hel)
 Hay, C. P., 109 (Typh)
 Hayman, J. M., Jr., 252 (Mal)
 Hazard, J. B., with Angevine, Hamilton & Wallace, 976 (Leish)
 Headlee, T. J., 763 (B.R.)
 Headsh, W. G., with Womersley, 28 (Typh), 324 (Ent)
 Hecht, O., 251 (Pl), 323 (Ent)
 — & Anduze, P. J., 463, 640 (Y.F.)
 Hegsted, D. M., McKibbin, J. M. & Stare, F. J., 784 (Mal)
 Hendelberger, M. & Mayer, M. M., 689 (Mal)
 Heilig, R. & Naidu, V. R., 80 (Typh)
 — & Vuveswar, S. K., 127 (Am), 442 (Mal)
 Heidman, F. R., with Kautson, M. & Greenburg, N., 893 bis (R.F.)
 Hersch, R. B., 658 (Misc. Dis)
 Helander, E. V., 512 (B.R.)
 Helander, S., 415 (Lab)
 Held, A., 113 (Typh)
 Heller, A. J., 387 (Ys)
 Heller, E. R., 579 (Hel)
 Helme, A. C. de B., 10 (Bl)
 Hemming, T., 244 (Mal)
 Hemming, G. R., 897 (Am)
 Henderson, A. B., with West, 253 (Mal)
 Henderson, C. A., 374 (Y.F.)
 Hennessy, R. S. E., 730 (Am)
 Henrad, C., van Wyneersch, H. & Wanson, M., (229) (Ent)
 —, with van Hoof & Peel, 96 (Tryp)

- Henry, A. J. & Grindley, D. N., 783 (Mal.)
 —, with Kirk, 18 (Leish.)
 Henschel, A., Taylor, H. I., Bruzek, J.,
 Mickelsen, O. & Keys, A., 145 (Heat Str.)
 Herrera, J. R., 265 (Typh.)
 Hertel, H. W., 496 (Misc. Dis.)
 Hertig, M. & Fisher, R. A., 758 (Ent.)
 Herzog, E., 676 (Rab.)
 Hess, A. D. & Hall, T. F., 626 (Mal.)
 — & Kiker, C. C., 183 (Mal.)
 —, with Kruse & Metcalf, 184 (Mal.)
 —, with Metcalf, 351 (Mal.)
 —, with Roseboom, 182 (Mal.)
 Hess, W. R., with Fetterman & Moran, 495
 (Misc. Dis.)
 Heyden, G., 491 (Oph.)
 Hiatt, E. P., 178 (Mal.)
 — & Quinn, G. P., 778 (Mal.)
 Hubbard, J. S., with Zuckerman, 480 (Hel.)
 Hicks, D. O., with Cram, 818 (Hel.)
 Hicks, J. D., 554 (Typh.)
 Hill, K. R., with Findlay & Macpherson, 289
 (Ys.)
 Hill, M. A. & Gordon, R. M., 940 (Ent.)
 Hindle, J. A., Rose, A. S., Trevett, L. D. &
 Prout, C., 446 (Mal.)
 Hurst, W. R. & McCann, W. J., 833 (Misc.
 Dis.)
 Hurt, G., 682, 683 (Rab.)
 Hoare, C. A., 559 (Am.)
 Hoare, E. D., 794 (Typh.)
 Hochstein, E., with Kellner & Tillman, (964)
 (Mal.)
 Hodes, P. J. & Keefer, G. P., 848 (Reports,
 etc.)
 Hodge, E. H. V., 630 (Mal.)
 — & Drew, R., 559 (Am.)
 Hodge, I. G., Denhoff, E. & Vander Veer,
 J. B., 1020 (Hel.)
 Hofer v. Lobenstein, M., (106) (Typh.)
 Hoffa, E., with Sorsby, 488 (Oph.)
 Hoffman, W. A., with Krakower & Axtmayer,
 133 (Hel.)
 Hogan, R. B., with Eagle, Doak & Steinman,
 15 (Tryp.)
 Hogue, M. J., 228 (Prot.)
 Holden, J. R. & Findlay, G. M., 503 (Ent.)
 —, with — & Markson, 6, 350 (Mal.)
 —, with Saunders & Hughes, 354 (Tryp.)
 Holdenried, R., with Burroughs, 387 (R.F.)
 Hole, N., 979 (Typh.)
 v. Hollósy, K., (219) (Hel.)
 Hoodless, D. W., 416 (Reports, etc.)
 van Hoof, L., Henrard, C. & Peel, E., 96
 (Tryp.)
 van Hoof, M. T., with Rodhain, (778) (Mal.),
 (791) (Tryp.)
 Hopkins, G. H. E., 230 (Ent.)
 Hopkins, H. U., with Fitz-Hugh & Pepper,
 340 (Mal.)
 Hopkins, R. & Faget, G. H., 737 (Lep.)
 Horne, S. F. & Harrell, G. T., 306 (Hel.)
 —, with —, (926) (Hel.)
 Horrenberger, R., with Durand, Beguet &
 Renoux, 107 (Typh.)
 — & Renoux, G., 107 (Typh.)
 —, with Sergeant, 365 (Typh.)
 Hou, H. C., 651 (Def. Dis.)
 — & Dju, M. Y., 650, (927) (Def. Dis.)
 Hou, P. C., (100) (Leish.)
- Howard, A. C., 10 (Bl.)
 Howat, H. T., 123 (Dys.)
 Howell, D. E., with Fischbach, (995) (Typh.)
 Howorth, M. B., 817 (Hel.)
 Ilisu, K. C., (41) (Am.)
 Ilse, L. T., 726 (Pl.)
 In, S. M. K., 918 (Hel.)
 Hudson, E. H., (863) (Mal.)
 Hudson, J. R., 678 (Rab.)
 Hudson, M. F., with Ladell & Waterlow, 143
 (Heat Str.)
 Huff, C. G. & Coulston, F., 538 (Mal.)
 Inffaker, C. B. & Back, R. C., 687 (Mal.)
 —, with Rice & Back, 632 (Mal.)
 Hughes, K. T. & Niesche, F. W., (628)
 (Mal.)
 Hughes, M. H., with Saunders & Holden, 354
 (Tryp.)
 Hühne, W., 447 (Mal.)
 Hume, W. E. & Szekely, P., 210 (R.F.)
 Hundley, J. M. & Nasi, K. W., 282 (Pl.)
 Hunt, A. R., 1019 (Hel.)
 — & Bloss, J. F. E., 969 (Tryp.)
 Hunt, R. S., (810) (Am.)
 Hunt, T. C., 5 (Mal.)
 Hunt, V. L., 766 (B.R.)
 Hunter, G. W., III, with Mackie & Worth,
 665 (D.R.)
 Huntington, R. W., Jr., with Fogel, 53
 (Hel.)
 Hurst, H., (941) (Ent.)
 Hurtado, A., Merino, C. & Delgado, E., 824
 (Haem.)
 Hussain, N., 881 (Typh.)
 Hyman, A. S., 962 (Mal.)
 Hynes, M., 822 (Haem.)
 —, Ishaq, M. & Morris, T. L., 651 (Haem.)

I.

- Ibarra, R., (44) (Lep.)
 Ibarra Perez, R. & Gonzalez Prendes, M. A.,
 (214), 1009 (Lep.)
 Ibbotson, C., with Menon, 884 (Typh.)
 Ignacio, L., with Magalhães, Coutinho,
 Gonçalves & Lucena, 1016 (Hel.)
 Ignacio Chala, H. J. & Lleras Restrepo, F.,
 566 (Lep.)
 Imrie, A. H., 169 (Rab.)
 India, 406 (Misc. Dis.), 822 (Haem.)
 Indian Med. Gaz., 30 (Typh.), 283 (Chl.)
 Inhelder, H. E., (862) (Mal.)
 Iriarte, D. R., 635 (Der.)
 Irons, E. N., with Kobls, Armbrust & Philip,
 993 (Typh.)
 Irons, J. V., Bohls, S. W., Thurman, D. C.,
 Jr. & McGregor, T., 462 (Typh.)
 Irvine, C., 406 (Ulc.)
 Irvine, K. N., with Macgrath, Brown,
 Rossiter, Lees, Parsons, Partington, Rennie
 & Havard, 251 (Mal.)
 Isaicheva, A. I., with Podypolskaya, 573
 (Hel.)
 Isbister, J., 749 (Sp.)
 Ishaq, M., with Hynes & Morris, 651 (Haem.)
 Isola, W. & Osimani, J. J. (230) (Ent.)
 Iswariah, V., (394) (Lep.)
 Iyengar, M. O. T., 625 (Mal.)

J.

- Jachowski, L. A., with Wilson & Matheison, 73 (Ent)
 Jack, R. W., 114 (Tryp.)
 Jackson, A. V., 244 (Mal)
 —, with Williams & Sinclair, 369 (Typh)
 Jackson, C. H. N., 186 (Tryp)
 — & Vanderplank, F. L., 187 (Tryp)
 Jackson, D. S., 881 (Typh)
 Jacob, J. E., with Tomlinson, 582 (Haem)
 Jacob, V. P., with Jaswant Singh, 618 (Mal)
 Jacobs, H. R., 465 (Y.F.)
 Jacobs, L., with Wright & Walton, 306 (Hel)
 Jacoby, A. H., London, J. R., Wyne, P. S. & Faulmeyer, T. R., 539 (Drs)
 Jaffe, H. L., 918 (Hel)
 Janes, S. P., 253, 630 (Mal), 282 (Chl), 845 (Reports, etc)
 Jang, C. S., 630 (Mal)
 Jansen, G., 1018 (Hel)
 —, with Nery Guimarães, 972 (Tryp)
 —, with Ponde & Mangabeira, 576, (Leish)
 Jarvis, J. F., 932 (Ulc)
 Jaswant Singh & Jacob, V. P., 618 (Mal)
 Javawardera, M. D. S., with Soysa, 320 (Misc Dis)
 Jeffery, G. M., 352 (Mal)
 Jellison, 405 (Ulc)
 Jellison, W. L., 805 (Pl)
 Jennings, R. K., 806 (Chl)
 — & Linton R. W., 378 bis (Chl)
 —, with —, 377 (Chl)
 Jettmar, H. M. & Shigan, L., 981 (Typh)
 Johnson, A. S., Jr., with Berry & Warshauer, 555 (Typh)
 Johnson, V. B., with Damon, 637, 990 (Typh)
 Johnson P. A. G., 478 (Hel)
 Johnson, R. E., with Pitts Consolano Poulin Razovk & Stachelek, 226 (Heat Str)
 Johnstone, D. F., 489 (Oph)
 Joki, F., 317 bis (Heat Str)
 de Jolmère, P. B., with Parrot, 662 (Ent)
 Jones, E. R., with Fiennes & Laas, 791 (Tryp)
 Jones, H., Rake, G. & Hamre D., 543 (Leish)
 Jones, M. F., with Cram & Wright, 646 (Hel)
 Jones, S. H. & Souders C. R., 149 (Misc Dis)
 Jones, V. P., with Maxwell, Coulston & Binckley, 839 (Prot)
 Jonescu D., 674, 677 (Rab)
 Jordan H. B., with Cantrell, 633 (Mal)
 Jörg M. E., with Mazza & Miyata, 792 (Tryp)
 Josephs, H. W., 61 (Haem)
 J Amer Med Ass., 799 (Typh)
 J Indian Med. Ass., 936 (Misc Dis)
 Jover, J., with Trespalacios, 212 (Lep)
 Jukota, N. N., 940 (Ent)
 Juon, M., 389 (Lep)

K.

- Kahali, B. S., with Gupta, J. C., 191 (Leish)
 Kahn, M. C., Celestin, W. & Offenhauser, W., 661 (Ent)
 Kaime, M., with Kessel, Allison, Quirros & Glycer, 40 (Am)

- Kalle, R. A., with Rao & Colah, 932 (Ulc)
 Kammer, V., 48 (Hel)
 Kanchaveh, G. L., 632 (Mal)
 Kane, F. F., 42 (R.F.)
 Kambolotskaya, L. N., with Steinberg & Karlova, 339 (Mal)
 Kanof, A., with Salzberger & Shaw, 1028 (Der)
 Kao, Y. E. & Chen, S. C., 756 (Misc Dis)
 Kaplan, A. & Landgren, A., 996 (Den)
 Kaplan, D., 735 (R.F.)
 Karlova, N. S., with Steinberg & Kambolotskaya, 339 (Mal)
 Kartagener, M., with Spühler, 1039 (Misc Dis)
 Kasimov, B., 50 (Hel)
 Kasperczak, K., with Siedek & Fanta, 105 (Typh)
 Kassirsky, I. A., 678 (Mal)
 Katsampas, C. P., with Farmer, 272 (Typh)
 Katzenellenbogen, I., 361 (Leish)
 Katzenstein, L., 899 (Ys)
 Kauntze, W. H., 255 (Mal)
 Kav, C. F., 696 (Mal)
 Keen, B. H., 359 (Leish), 420 (Reports, etc)
 — & Smith, J. A., 338 (Mal)
 Keeler, G. P., with Hodes, 848 (Reports, etc)
 Keegan, H. L., with Olson, 504 (Ent)
 Keh-Wei-Huang, 69 (Misc Dis)
 Keil H., with Bechthel & Rothberg, 900 (Lep)
 Kellin D., 150 (Ent)
 Kellner, A., Hochstein, E. & Tillman, A. J. B., 964 (Mal)
 Kennaway, L. L., 150 (Misc Dis)
 Keon-Cohen B. T., with Lawes, 234 (Reports, etc)
 Kern, R. A. & Norris R. F., 341 (Mal)
 Kessel, J. F., Allison, D. K., Kaime, M., Quirros, M. & Gloeckner, A., 40 (Am)
 Kessler, W. R. & Zwemer, R. L., 889 (Bart)
 Kers, A., with Henschel, Taylor, Brozek & Mickelsen, 145 (Heat Str)
 Khan H., 92 (Mal)
 Khan N. C., 861 (Mal)
 Khokhlova Buyanova, O. F., 230 (Ent)
 Khodukin N. I., 356 (Leish)
 Khramushin J. E., with Pchenichnov, 3 bis (Ent)
 Kjaer, W., with Petri & Norgaard, 3 (Def Dis)
 Kiang L., with Kuo, 741 (Hel)
 Kibler, M., 639 (Typh)
 Kiker, C. C., with Hess, 183 (Mal)
 Kikuth W., 102 (Leish)
 King, B. G., 304 (Hel)
 King, E. J. & Gilchrist, M., 781, 782 (King, G., 845 (Reports, etc)
 King, H., 971 (Tryp)
 —, with Andrews, van den End Walker, 20 (Typh)
 Kirby, H., 838 (Prot)
 Kirk, R., 190, 875 (Leish)
 — & Bayoumi, A., 374 (Y.F.)
 — & Henry, A. J., 18 (Leish)
 Kirkaldy-Willis, W. H., 740 (Lep)
 Kuman, B. H., with Comerford, 522 (Dis)
 Kurwan, E. O'G., Sen, K. & Bose, 2 (Oph)
 Kitchen, S. F., with Boyd, 174 (Mal)

- Kleinhaus, E. M., with Lyon, 1040 (Misc. Dis.)
 Kleinman, A., Page, R. C. & Preisler, P. W., (829) (Yms.)
 Khler, I. I., with Birnbaum & Goldblum, 700 (Bl.)
 Khler, I. J., Guggenheim, K. & Schwartz, I., 930 (Heat Str.)
 — & Oleinik, E., 23 (Typh.)
 Klitzner, H., 455 (Leish.)
 Klopstock, A. & Steinitz, H., 590 (Misc. Dis.)
 Knight, K. L., Bohart, R. M. & Bohart, G. L., 511 (B.R.)
 — & Farner, D. S., 638 (Mal)
 Knipe, F. W., with Russell, Ramachandria Rao & Patnam, 687 (Mal.)
 Knippling, E. F., with Bushland & Eddy, 660 (Ent)
 — & Dove, W. E., 660 (Ent)
 —, Gjullin, C. M. & Yates, W. W., 73 (Ent)
 —, with Lindquist & Schroeder, 1044 (Ent)
 —, with Madden & Lindquist, 73 (Ent)
 Knott, J. I., 497 (Misc. Dis.)
 Knutson, M., with Heilman & Greenburg, 898 bis (R.F.)
 Koepfli, J. B., with Mead, 9 (Mal)
 Kohls, G. M., Armbrust, C. A., Irons, F. N. & Philip, C. B., 993 (Typh.)
 —, with Blake, Maxcy, Sadusk & Bell, 991, 993 (Typh.)
 —, with Cooley, 154 (B.R.)
 Kojevnikov, P. V., 876 (Leish.)
 Kojevnikova, E. V., 454 (Leish.)
 Kondi, A., with Foy, Rebelo & Soeiro, 634 (Bl.)
 Korshunova, O. S., 274 (Typh.)
 —, with Skorin, 638 (Typh.)
 Kossoraja, E. M., with Alisov, 989 (Typh.)
 Kourf, P., 477 (Hel)
 Kovács, G. & v. Kup, J., 461 (Typh.)
 Krakower, C., Hoffman, W. A. & Axtmayer, J. H., 133 (Hel.)
 Kremer, H., with Ruge, 85 (Mal)
 Krick, E. S., with Vonfraenkel, 592 (Misc. Dis.)
 Krikorian, K. S., with van Rooyen & Bowie, 264 (Typh.)
 Krontovskaya, M. K. & Shmatikov, M. D., 274 (Typh.)
 Kruse, C. W., Hess, A. D. & Metcalf, R. L., 184 (Mal)
 Kubes, V., 422 (B.R.), 454 (Tryp)
 Kudo, R. R., 327 (B.R.)
 Kuhn, M. J., with Savino & Morales Villazon, 558 (Pl.)
 Kunstadter, R. H. & Prendergrass, R. C., (655) (Der)
 Luo, P. T., with Chu & Chang, (927) (Def. Dis.)
 Luo, S. & Kiang, I., 741 (Hel)
 —, Kup, J., with Kovács, 461 (Typh.)
 Laha, P. N., 936 (Misc. Dis.)
 —, with Gupta, 87 (Mal)
 Lahuri, S. C., 643 (Chl)
 Laird, R. L., with Coggeshall & Porter, 699 (Mal)
 Lal, H. B., 590 (Misc. Dis.)
 Lam, C. R., with McClure, 627 (Mal.)
 Lamb, W. L. & Royston, G. R., 561 (Am.)
 Lampert, H., 365 (Typh.)
 Lancet, 68, 342, 779 (Mal), 680 (Rab)
 Lane, C., 400 (Hel)
 Langer, K., 76 (Reports, etc.)
 Langer, P., Martin H. & Muller, P., 499 (Ent)
 de Laosa, O., with Frespalacios & Gonzalez Peris, 586 (Der)
 Lapping, 405 (Ulc)
 Larsh, J. F., Jr., 322 (Prot)
 Laser, H., (219) (Hel)
 Laskin, 795 (Typh.)
 Latenda, R. I. & Carpanelli, J. B., 137 (Hel)
 Laure, G., 267 (Typh.)
 Lavoipierre, M., with Golberg & de Meillon, (1043) (Ent)
 —, with de Meillon & Golberg (1043) (Ent)
 Laves, C. H. W. & Keon-Cohen, B. T., (234) (Reports, etc.)
 Laws, S. G., with Fienness & Jones, 791 (Tryp)
 Lawton, A. H., with Brady, Cowie, Andrews, Ness & Oorden, 747 (Hel)
 Leão, A. E. A., with da Cunha, Guimarães & Cardoso, 1003 bis (Y.)
 Leckie, M. W., with Browning & Calver, 709 (Tryp)
 Ledent, H., 75 (Reports, etc.)
 Leilentu, (172) (Mal)
 Lee, C. U., with Chung & Wang, (876) (Leish.)
 Lee, D. H. K., 76 (Reports, etc.)
 Lee, D. J. & Woodhall, A. R., 1049 (B.R.)
 Lee, R. K. C. & Pang, H. Q., 593 (Misc. Dis.)
 Lee, R. V., 313 (Der)
 Lees, J. C., with Macgrath, Brown, Rossiter, Irvine, Parsons, Partington, Reanne & Harvard, 251 (Mal)
 Lefèvre with Grosflez, (1038) (Misc. Dis.)
 LeFevre, I. D., Jr., McDermott, K. F. & Venner, R. B., 470 (Ys)
 Leikowitz, M. & Sukiennik, S., 591 (Misc. Dis.)
 Le Gall, R., (215) (Hel), (233) (Reports, etc.), 280 (Pl)
 Leitman, M. Z., 254 (Mal)
 Lemaire, G., 268 (Typh.)
 Lennette, E. H. & Perlowagora, A., 802 (Y.F.)
 —, with —, 114 (Y.F.)
 Lent, H., 973 (Tryp)
 — & de Oliveira, S. J., 973 (Tryp)
 León, A. P., 193, 202, 984 (Typh.)
 Leon y Blanco, F. & Angel Abalo, M., 225 (Der.)
 — & Oteiza, A., 585, 750 (Der.)
 —, with Soberón y Parra, 1027 (Der)
 Leprosy in India, (291), 739, 1005 (Lep)
 Leprosy Review, (1013) (Lep.)
 Leslie, A., with Silverman, 1001 (Am.)
 Lester, H. M. O., 788 (Tryp)

L.

- adell, W. S. S., Waterlow, J. C. & Hudson, M. F., 143 (Heat Str.)
 aender, J. F., with Lopes, 979 (Leish.)
 agos, Nigeria, 800 (Y.F.)

- Leventhal, L., with Stryker & Halbensen, 531 (Def. Dis.)
 Lever, R. J. A. W., 778 (Mal), 938 (Ent.)
 Levine, H. D., 556 (Typh.)
 Levkovich, E. N., 268 (Typh.)
 — & Petrusheva, P. A., 268 (Typh.)
 Levy, B. & Black-Schaffer, B., 833 (Der.)
 Lewis, B. O., with Sodeman, 562 (Am.)
 Lewis, D. J., 246 (Mal), 1042 (Ent.)
 Lewis, J. A., 405 (Ulc.)
 Lewis, R. A., 443 (Mal)
 —, with Senekue, 977 (Leish.)
 Lewthwaite, R., 887, 979 (Typh.)
 Lewy, R. B., 1035 (Oph.)
 Li, C. C., with Politzer, 726 (Pl.)
 Li, C. H., with Chang, Tong & Chin, 744 (Hel.)
 Liebermann, H. R., 894 (Am.)
 Liew, V. T., 878 (Leish.)
 Lillie, R. D., 414, 662 (Lah.)
 Lima, S., with Soper, Wilson & Antunes, 79 (B.R.)
 Lindgren, A., with Kaplan, 996 (Den.)
 Lindquist, A. W., with Madden & Knaphing, 73 (Ent.)
 —, Schroeder, H. O. & Knaphing, E. F., 1044 (Ent.)
 Linhares, H., 277, 278 bis, 279, 373 (Y.F.)
 309 (Vim.), 394, 395, 473, (904), 1014 (Lep.)
 —, with Villela, (214) (Lep.)
 Linskus, D. Y., 888 (Typh.)
 Linton, R. W. & Jennings, R. K., 377 (Chl.)
 —, with —, 378 bis (Chl.)
 Lippman, B. L., Casey, A. V., Byron, R. A. & Evans, E. C., 371 (Typh.)
 Lippincott, S. W., with Gordon, Marble, Hall, Ellersbrook & Glass, 692 (Mal.)
 Lipscomb, L. L. & McMahon, J. L., 804 (Den.)
 Lisboa, A., 817 (Hel.)
 Liu, W. T., 719 (Typh.)
 Liu, Y. P., with Cheng & Tan, 733 (Am.)
 Livesav, H. R. & Pollard, M., 203 (Typh.)
 Lleras Restrepo, F., with Ignacio Chala, 566 (Lep.)
 Loewenstein, A., with McGregor, 91 (Mal.)
 Lofgren, R. C., 388 (Ys.)
 Legue, J. B., 274 (Typh.)
 Longley, E. O., 979 (Typh.)
 Lopes, C. F. & Laender, J. F., 979 (Leish.)
 Löscher, H., with Beiglböck, 31 (Typh.)
 Loudon, J. R., with Jacoby, Wyne & Faulmerger, 559 (Dys.)
 Lourie, E. M., 539 (Am.)
 Louw, A. & Nielsen, H. E., 60 (Haem.)
 Low, G. C., 843 (Reports, etc.)
 Lowe, J., 711 (Leish.)
 Lozano Hube, E., with Mazroti, 55 (Hel.)
 Lucas, R. B., 886 (Typh.)
 Lucena, D., with Maralhões, Coutinho Gouveia & Ignacio, 1016 (Hel.)
 Luis Carr, E., (810) (Am.)
 Luis Dao L., 17, 711 (Tryp.), 697 (Mal.)
 Lurie, H. I., 824 (Haem.)
 Lwoff, M. & Nicolle, P., (189) (Tryp.), (842) (Ent.)
 —, with —, (189) (Tryp.)
 Lvon, E. & Kleinhaus, E. M., 1040 (Misc. Dis.)
 McAllister, J., with Augustine & Weinmar, 288 (R.F.)
 McCann, W. J., with Hurst, 838 (Misc. Dis.)
 McCann, W. S., with Sellards, 115 (Y.F.)
 McCarthy, D. D., with Annecke & Wilson, 966 (Mal.)
 Macchavello, A., 103 (Typh.)
 — & Unguen, D., 466 (Pl.)
 McClure, R. D. & Lam, C. R., 627 (Mal.)
 McCombie, 405 (Ulc.)
 McConaghey, R. M. S., 730 (Am.)
 McCorkle, J. K., 536 (Mal.)
 McCoy, O. R., (229) (Ent.), 433, 785 (Mal.)
 McCreary, J. F. & Tisdall, F. I., 58 (Def. Dis.)
 McCulloch, R. N., 369 (Typh.)
 McDaniel, G. E., with Faust & Scott, 62 (Mal.)
 McDermott, K. F., with LeFevre & Venner, 470 (Ys.)
 Macdonald, G., 630, 965 (Mal), 839 (Ent.)
 McDonald, S., with Bingham, 305 (Hel.)
 McDonald, S. F., 371 (Typh.)
 McFarlane, A. L. & Branday, W. J., 755 (Misc. Dis.)
 Macfie, J. W. S., 244 (Mal.)
 McGann, V. G., with Burrows, Mather & Wagner, 727 (Chl.)
 McGavack, T. H. & German, W. M., 141 (Haem.)
 McGinn, S. & Carmody, J. T. B., 341 (Mal.)
 Macgregor, I. M., 413 (Ent.)
 Macgregor, I. S. & Loewenstein, A., 91 (Mal.)
 McGregor, M., 417 (Reports, etc.)
 McGregor, T., with Irons, Bohls & Therman, 462 (Typh.)
 McHardy, G., with Browne & Spellberg, 729 (Am.)
 MacIntosh, R. M., with Chen & Geising, 869 bis, 872 (Tryp.)
 Machella, T. E. & Forrester, J. S., 994 (Typh.)
 McIndoo, N. E., with Roark, 841 (Ent.)
 Mackay-Dick, J., 377 (Pl.), (977) (Leish.)
 McKee, R. W., with Ball, Anfinson, Geiman & Ormsbee, 867 (Mal.)
 Mackenzie, G. K., with Ferriman, 124 (Dys.)
 McKibbin, J. M., with Hegsted & Starr, 784 (Mal.)
 MacKichan, I. W., 18 (Tryp.)
 Mackie, J. W., 417 (Reports, etc.)
 Mackie, T. T., Hunter, G. W., 111 & Worth, C. B., 665 (B.R.)
 McLanahan, R. F., with Michael & Cenar, 66 (Der.)
 McLanahan, R. R. M., 1027 (Der.)
 McLanahan, R. E. & DeVecho, S. B., 506 (Lab.)
 McMahon, J. L., with Lipscomb, 804 (Den.)
 McNaughton, F., with Anderson & Begg, 497 (Misc. Dis.)
 Macpherson, A., with Findlay & Hill, 28 (Ys.)
 Macquade, D. H. G., 145 (Heat Str.)
 McSweeney, A., with Flecker, 66 (Der.)
 Madden, A. H., Lindquist, A. W. & Knaphing, E. F., 73 (Ent.)

- Maegraith, B. G., 10 (Bl), 64 (Vms.), 630 (Mal),
788 (Bl.)
—, *et al.*, 760 (Mal.)
—, Brown, G. M., Rossiter, R. J., Irvine
K. N., Lees, J. C., Parsons, D. S.,
Partington, C. N., Rennie J. L. & Havard,
R. E., 251 (Mal.)
— & Findlay, G. M., 12 (Bl)
— & Havard, R. E., 12 (Bl.), 863 (Mal)
—, — & Parsons, D. S., 968 (Bl)
Magalhães, A., Coutinho, B., Gouveia, L.,
Lucena, D. & Ignacio, L., 1016 (Hel)
Magalhães, B. F. & Dias, C. B., 1016 (Hel)
de Magalhães, O. & Rocha, A., 986, 988
(Typh.)
Magnusson, H. J., with Eagle, 356 (Tryp)
Mahaffy, A. F., with Smithburn & Haddow,
321 (Misc. Dis.)
Mahmoud, A. H., 412 (Prot.)
Malevsky, with Ravikovich, Starovierova &
Neuman, 549 (Typh.)
Malevsky, M. M., with —, — & Ratner,
549 (Typh.)
Mar, L. P., 944 (B.R.)
Majumder, D. N. & Das Gupta, C. R. (141)
(Haem.)
Malhotra, R. P. & Chhuttani, P. N., 59
(Haem.)
Malone, R. H. & Brooks, A. G., 357 (Leish)
Mandekos, A., 501 (Ent.)
Mangabeira, O., Jr. & Galindo, P. (151) (Ent)
—, with Pondé & Jansen, (876) (Leish)
Mann, I., 826 (Haem.)
Manson-Bahr, P., 10 (Bl.), 176 (Mal), 207
559 (Am.), 762 (Misc.), 845 (Reports, etc.)
— & Muggleton, W. J., 325 (Ent.), 431
(Mal)
Manson-Bahr, P. E. C. & Gnyer, O. K. G.,
409 (Misc. Dis.)
Mantilla, L. R., with Rivas & Góbbich, 910
bis (Hel.)
Manwell, R. D., Coulston, F., Binckley, E. C.
& Jones, V. P., 839 (Prot.)
Mao, C. P., with Yu, 747 (Hel)
Marble, A., with Gordon, Lippincott, Ball,
Ellerbrook & Glass, 692 (Mal)
Marchionini, A., 310 (Der.)
Mariani-Tosatti, G., 498 (Misc. Dis.)
Mariano, J., 133, 1010 (Lep.)
—, with de Oliveira Castro, 1009 (Lep.)
—, with de Souza-Araujo & de Oliveira
Castro, 1009 (Lep.)
Mariotte, C. O., Bustamante, M. E. &
Varela, G., 721 (Typh.)
Markell, E. K., 468 (Am.)
Markson, J. L., with Findlay & Holden, 6,
350 (Mal.)
Marneffe, H., Ranque, J. & Sautet, J., 247
(Mal.)
—, with Sautet, 336 (Mal.)
Marques, A., 209 (R.F.)
Marnott, H. L., 753 (Misc. Dis.)
Marsh, F., 493 (Heat Str.)
— & Wilson, H. A., 583 (Ulc.)
Marshall, J. M., 438 (Mal.)
—, with Walters, Watkins & Butt, 37
(Am.)
Martin, A. P., 78 (B.R.)
Martin, H., with Länger & Moller, 499 (Ent.)
— & Wain, R. L., 152 (Ent.)
Martin, L. A., with Blanc & Baltazard 713
(Typh)
Martin, R., (324), 414 (Ent.)
— & Debey, M. 37 (Am.)
Martin W. B., with Coggeshall & Bates 698
(Mal)
Martins, A., Versiani, V. & Tupinambá, A.,
(875) (Tryp)
Marx, R., with Aschenbrenner, 105 (Typh)
Masen J. M., 8 (Mal)
Mason A. S., with Ward, 934 (Ulc.)
Mason, E. D., 227 (Heat Str.)
Master A. M., 657 (Misc. Dis.)
Mater, D. A., with Freis 402 (Tryp)
Mather A. V., with Burrows & Wagner, 728
(Chl)
—, with — & McGann 727 (Chl)
Matheson, D. R., with Stoll & Ward, 999
(Am)
—, with Wilson & Jachowski 74 (Ent)
Matoff, K., 579 (Hel)
Mattingly, P. I., 434 (Mal)
Maveety, H. M., Turnbull, R. B., Jr. &
Bauer C. R., 441 (Mal)
Maxcy, K. F., with Blake, Sadusk Kohls &
Bell, 991, 993 (Typh)
May, W. K. C., 735 (R.F.)
Mayer, M. M., with Heidelberg, 689 (Mal)
Mayer, R. A., with Di Giacomo, 47 (Hel)
Mazza, S., Miyara, S. & Joré, M. E., 792
(Tryp)
Mazzotti, L., 134, 219, 398, 647, (926), (Hel)
— & Lozano Hube L., 55 (Hel)
Mead, J. & Koepfli, J. B., 9 (Mal)
Measham, J. E., Yoeh, M. & Finnegan, J. D.,
695 (Mal)
Medical Clinics of North America, 765 (B.R.)
Medical Research Council, 843 (Lab.), 1052
(B.R.)
Medlicott, R. W., 581 (Def. Dis.)
Megaw, J. W. D., 506 (Reports etc.), 797
(Typh)
de Meillon, B., Golberg, L. & Lavoipierre, M.,
(1043) (Ent)
—, with — & —, (1043) (Ent)
—, Parent, M. & Black, L. O. C., (940)
(Ent)
Meira, J. A. & Ramos, J., Jr., 572 (Hel)
de Meira, M. T. V. & Ferreira, T. G., (1044)
(Ent)
Mellanby, K., 839 (Ent)
de Mello, R. P., with Cruz, 1020 (Hel)
Mendelsohn, H. V., 66 (Der)
Menon, I. G. K., 589 (Misc. Dis.)
Menon, M. C. & Ibbotson, C., 834 (Typh)
Menzies, T. H., with Anderson, von Desch-
wanden & Gray, 961 (Mal)
Merno, C., with Hurtado & Delgado, 824
(Haem.)
Merrill, B. R., 691 (Mal.)
Merrill, E. D., 234 (B.R.)
Mestre Myares, J. J., 43 (Lep)
Metcalf, R. J. & Ungar, J., Jr., 341 (Mal)
Metcalf, R. L. & Hess, A. D., 351 (Mal.)
—, with Kruse & Hess, 184 (Mal)
Meyer, H., with Romaña, 972 (Tryp.)
Meyer, K., with von Sallmann & Di Grandi,
489 (Oph)
Michael, P., McLaughlin, R. F. & Cenac,
P. L., 66 (Der.)

- Mickelsen, O., with Henschel, Taylor, Brozek & Keys, 145 (Heat Str.)
 Miles, V. I., with Coatney & Cooper, 865 (Mal.)
 Miller, H., (411) (Misc. Dis.)
 Müller, J. F. & Einhorn, N. H., 578 (Hel.)
 —, with — & Whittier, 911, 912, 914 (Hel.)
 Müller, M. H., with Whitehall, 576 (Hel.)
 Mills, C. A., 930 (Heat Str.)
 Milne, R. I., (996) (Typh.)
 Mina, H., 494 (Ulc.)
 Mingoja, Q., 632 (Mal.)
 Minnich, V., with Moore, Vilter & Spies, 482 (Haem.)
 Minton, J., 1037 (Oph.)
 Miranda, R. N., 1011 (Lep.)
 —, with de Souza-Araujo, 1007 (Lep.)
 Misra, K. N., 120 (Chi.)
 Mitterstein, B. & Stern, H. J., 1030 (Oph.)
 Mitscherlich, E., 78 (Reports, etc.)
 Miyara, S., with Mazza & Jörg, 792 (Tryp.)
 Mohammed, A. H., 583 (Vms.)
 Moiser, B., 294 bis (Lep.)
 Mole, R. H., 1023 (Haem.)
 Mom, A. M. & Basombrio, G., 1012 (Lep.)
 Mochadskil, A. S., with Blagoveschenskoi & Bregetova, 230 (Ent.)
 Money, T. D. F., 392 (Lep.)
 Monning, H. O., 401 (Hel.)
 Monro, H. A. U., Brand, L. J., Delisle, R. & Smith, C. C., 759 (Ent.)
 Monthly Bull. Ministry of Health & Emergency Pub. Health Lab. Service, 680 (Rab.), 879 (Typh.)
 Montoya, J. A., 551 (Typh.)
 Montpelier, J. & Catanei, A., 67 (Der.)
 Moore, C. V., Vilter, R., Minnich, V. & Spies, T. D., 482 (Haem.)
 Mosser, H., 500 (Ent.)
 Moragues, V., with Greiff & Pinkerton, 362 (Typh.)
 Morales Villazon, N., with Savino & Kuhn, 558 (Pl.)
 Moran, T. J., with Fetterman & Hess, 495 (Misc. Dis.)
 Morehead, J. F., 720 (Typh.)
 Morgan, C. N., 124 (Am.)
 Morris, J. N., 941 (Reports, etc.)
 Morris, T. L., with Hynes & Isbaq, 651 (Haem.)
 Morrison, D., with Greenslade, (229) (Prot.)
 Morrison, D. B., with Dularey, 352 (Mal.)
 Morton, H. L. & Engley, F. B., Jr., 997 (Dys.)
 Morton, T. C. St. C., 731 (Am.)
 Moshkovski, S. D., (622) (Mal.)
 Mountz, A., (814) (Lep.)
 Moustardier, G. & Nicol, R., 933 (Ulc.)
 Mozley, A., 516 (B.R.)
 Mudrow, L. & Schultz, F., 814 (Lep.)
 Muggleton, W. J., with Manson-Bahr, 325 (Ent.), 434 (Mal.)
 Mugrage, L. R., with Florio & Stewart, 118 (Den.)
 —, with Stewart & Florio, (119) (Den.)
 Muur, E., 390 *ter*, 1004 (Lep.)
 Mukerji, A. K. & Bhaduri, N. V., 919 (Hel.)
 Mukerji, B., with Pal, Gupta & Chatterjee, 286 (Am.)
 Mukherji, N., with Dharmendra, 900, 903 (Lep.)
 Mulhens, K., 502 (Ent.)
 Müller, H. K., 548 (Typh.)
 Muller, P., with Länger & Martin, 499 (Ent.)
 Mulrennan, J. A., Goodwin, M. & Shannon, R. C., 633 (Mal.)
 Mum, J., & De Freitas, G., 975 (Tryp.)
 Mauter, E. J., 805 (Pl.)
 Murphy, R. C., Jr. & Shapiro, S., 58 (Haem.)
 Murray, E. S., with Yeomans, Snyder, Zafalonetis & Eecke, 201 (Typh.)
 Mushett, C. W., with Siegel, 178 (Mal.)
 —, with — & Emerson, 628 (Mal.)
- N.
- Nabokov, V. A., 1045 (Ent.)
 Naftalin, J. M., with Graham, 676 (Leish.)
 Nagibina, N. I., with Varygin, 349 (Mal.), 989 (Typh.)
 Naidu, V. R., with Heilig, 30 (Typh.)
 Nauman, D. N., (100) (Tryp.)
 Najera Angulo, L., 130 (R.F.)
 Najjar, V. A., with Roberts, 56 (Def. Dis.)
 Napier, L. N., 79 (B.R.)
 Nargund, K. S., with Paranjape, Phalnikar & Bhade, 571 (Hel.)
 Nasr, K. W., with Handley, 282 (Pl.)
 Natarajan, B., with Viswanathan, 411 (Misc. Dis.)
 Neel, J. V., with Valentine, 223, 825 (Haem.)
 Neeman, M., (91) (Mal.)
 Neghme, A., 453 (Tryp.)
 Negroni, P. & Bonfiglioli, H., 586 (Der.)
 Nelson, J. H. & Cruickshank, J. C., 363 (Typh.)
 Nelson, N., with Eichna, Bean & Ashe, 751 (Heat Str.)
 Nery Guimarães, F. & Jansen, G., 972 (Tryp.)
 Ness, A. T., with Brady, Lawton, Cowie, Andrews & Ogden, 747 (Hel.)
 Nettel, R., 54 (Hel.)
 Neuda, P. M. & Rosen, M. S., 825 (Haem.)
 Neuman, A. S., with Ravikovich, Staroverova & Maevsky, 549 (Typh.)
 —, with —, —, — & Ratner, 549 (Typh.)
 Nicol, L., with Ramon, Boquet, Richon & Delaunay-Ramon, (584) (Vms.)
 Nicol, R., with Moustardier, 933 (Ulc.)
 Nicolle, P. & Lwoff, M., (189) (Tryp.)
 —, with —, (189) (Tryp.), (842) (Ent.)
 Nielsen, H. E., with Louw, 60 (Haem.)
 Niesche, F. W., with Hughes, (628) (Mal.)
 Nigeria, 790 (Tryp.)
 Niño, F. L., 473, 909 (Hel.)
 Norgaard, F., with Petri & Kiaer, (308) (Def. Dis.)
 Norris, R. F., with Kiern, 341 (Mal.)
 North, J. P., with Ravdin, (964) (Mal.)
 Notestem, F. W., 507 (Reports, etc.)
 Nutrition Reviews, New York, 8 (Mal.)
 Nyasaland Protectorate, 583 (Ulc.)

O.

- Obermayer, M. E. & Frost, K., 832 (Der.)
 O'Brien, J. P., with Allen, 313 (Heat Str.)
 O'Bryan, B. E., with Schuhardt, 387, 735, (R.F.)
 O'Connor, N., 218 (Hel.)
 Offenhauser, W., with Kahn & Celestin, 661 (Ent.)
 Officer, R., 688 (Mal.)
 Ogden, G. E., with Brady, Lawton, Cowie, Andrews & Ness, 747 (Hel.)
 Olarte, J., with Varela & Castro Estrada, 927 (Der.)
 Olavarna, J., with Clavero, (859) (Mal.)
 Oldfield, M. C., (250) (Mal.)
 Oleinik, E., with Khigler, 23 (Typh.)
 de Oliveira, J. C. & de Bettencourt, A., 166 (Rab.)
 Oliveira, S. J., with Lent, 973 (Tryp.)
 Oliveira Castro, G. M., 960 (Mal.)
 —, & Mariano, J., 1009 (Lep.)
 —, with de Souza-Araujo & Mariano, 1009 (Lep.)
 Oliver-González, J., 353 (Bl.)
 — & Bercovitz, Z. T., 219 (Hel.)
 — & Torregrossa, M. V., 45 (Hel.)
 Olsen, O. W., (302) (Hel.)
 Olson, T. A. & Keegan, H. L., (504) (Ent.)
 Ordsman, D., 41 (R.F.)
 Ormsbee, R. A., with Ball, Anfinsen, Geiman & McKee, 867 (Mal.)
 Osburn, H. S., 285 (Am.)
 Osburn, L. W., 455 (Typh.)
 Osimani, J. J., with Isola, (230) (Ent.)
 Osorno-Mesa, E., with Boshell-Manrique, 114 (Y.F.)
 Ostrovskaya, S. G., with Vainberg, Gula-mova, & Perekrstostova, 549 (Typh.)
 Oteiza, A., 584 (Der.)
 —, with Léon-Blanco, 585, 750 (Der.)
 Ott, W. H., with Seeler, 540 (Mal.)
 Quary, G., with Hamm, 495 (Ulc.)
 Ovchinnikova, L. M., (595 bis) (Ent.)
 Osburn, R. H., (229) (Ent.)

P.

- ackchanian, A., (74) (Ent.)
 age, R. C., with Kleinman & Preisler, (829) (Vms)
 ai, M. N., 942 (Reports, etc.)
 Akenham-Walsh, R., 400 (Hel.)
 al, J. C., Mukerji, B., Gupta, J. C. & Chatterjee, M. L., 286 (Am.)
 Palmer, E. D., 135 (Hel.)
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